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Section of Balneology and Climatology.

[*January* 17, 1930.]

Tissue Reaction in Disorders of the Rheumatic Group: with particular reference to Subcutaneous Nodules.

By Vincent Coates, M.C., M.D.

This paper is proffered as another link in the chain of evidence which is tending to establish the relation of orthodox rheumatic infection to multiple infective arthritis of unknown origin. This relationship is thought to be such that both these disorders are but varied expressions of the same disease; circumstance, organ inferiority, and immunity deciding the site of election and the exuberance of the reaction.

Before proceeding further it is only reasonable to offer a short explanation as to why all types of non-specific polyarthritis are grouped together as a whole. Until recent date it was the custom to do this in Great Britain, and in America it is the rule rather than the exception to divide multiple non-specific, non-suppurative arthritis into atrophic and hypertrophic categories. Though it is good practice to recognize different clinical types and not difficult to demonstrate the outstanding difference between a fully established "atrophic" case—with its profound metabolic disturbance, symmetrical fusiform polyarthritis, enlarged spleen and glands, achlorhydria and anæmia without discoverable foci of infection—and a mild case with little or no systemic disturbance, arthritis of scattered distribution, absence of gross dislocation of the homopoietic mechanism and obviously septic teeth, yet it is another affair to decide exactly where the so-called "atrophic" or "true rheumatoid" case ends and other forms begin, when, say, twenty-five cases are seen side by side, each displaying only a degree less disability than the last. Again, the aspects of disease change from time to time. The so-called "atrophic" case of to-day is the less advanced case of to-morrow, and vice versa. And this is only to be expected, for what two individuals show the same systemic or local disturbance in any given infection? Would not either every case of rheumatic fever develop mitral stenosis, or else this complication remain unknown? It would be good policy to visualize the clinical types of arthritis under review as being "severe," "moderately severe," or "formes frustes."

The reasonableness of allying orthodox to heterodox rheumatic infection is based upon two main principles. In general, the well recognized fact that many disorders of an infective nature are prone to exhibit widely divergent manifestations: in particular, the merging of one condition into the other, the occurrence of common symptoms, complications and cardinal signs. Syphilis, with its protean and ubiquitous attack upon joints, bones, viscera and nervous system, may be instanced

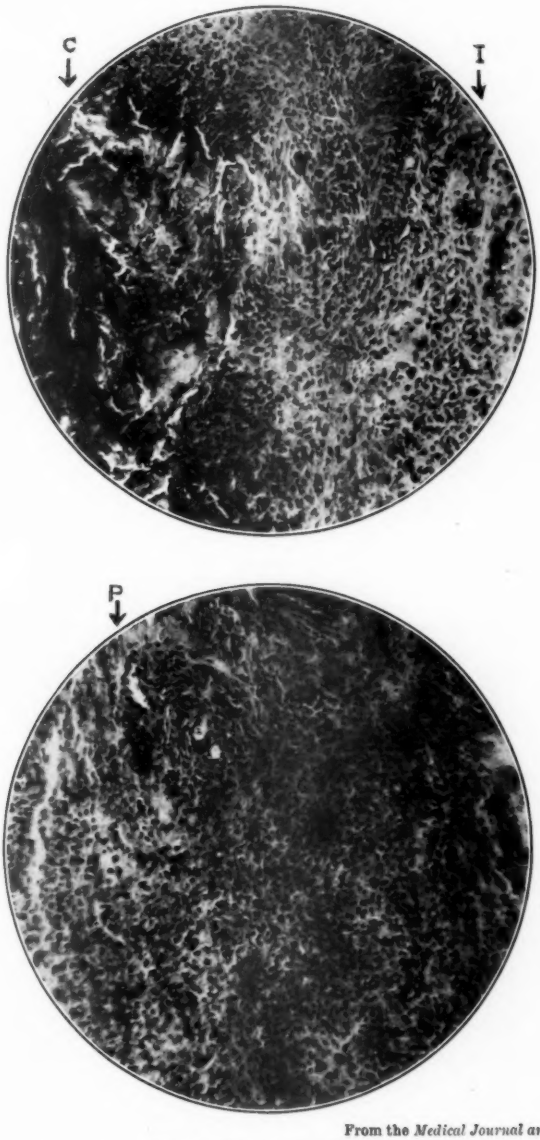
as an example of the first principle, and the familial [1] and personal history of rheumatic fever, the subcutaneous nodules and carditis of orthodox type in cases of infective arthritis, as an example of the second.

How then does tissue reaction help to consolidate or refute the suggestion that orthodox and heterodox infection are related?

It is now an established custom to diagnose certain types of disease by histological examination, even after failure to incriminate known or unknown organisms. Thus a lesion can be estimated as being syphilitic or tuberculous, and not infrequently such widely differing conditions as lymphadenoma, gonorrhœal salpingitis and amœbic colitis can be correctly diagnosed by their histological patterns. It is proposed therefore to reorganize the pathological data available in such a manner as to present what is claimed to be a reaction specific, not only for orthodox, but also for heterodox rheumatic infection.

(1) *The stages by which the conclusion has been reached that orthodox rheumatic infection gives a specific tissue reaction.*

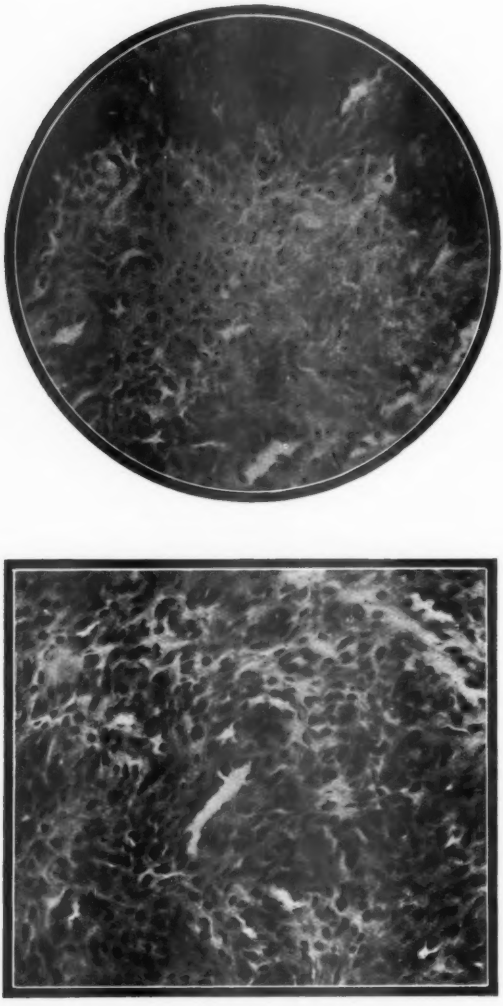
Sauvages [2] in the second half of the eighteenth century, is stated to have been the first to describe subcutaneous nodules, but Froriep [3] is probably actually the first observer who associated these with rheumatic disorders. Though various other writers, prior to 1881, described subcutaneous nodules, it is to Barlow [4] and Warner that we owe not only the classical description, but the statement that "Such nodules belong strictly to the fibrous tissues, and in nature are probably homologous with the inflammatory exudate which forms the basis of a vegetation on a cardiac valve." The discovery of the submiliary nodule in the rheumatic myocardium by Geipel [5] in 1905 and by Aschoff [6] in 1906 was the next important discovery, though Poynton and Still [7] in 1899 had drawn attention to the inflamed areas in the serous membranes of active rheumatic carditis. In 1911 Carey Coombs [8] was able to point out that the histological elements of the subcutaneous nodule, the submiliary nodule, the serous membranes of the heart and the synovial membrane of joints affected by rheumatic fever were identical. In 1925 Coates [9] described subcutaneous millet-seed granules in subacute rheumatic children which histologically were pocket editions of the subcutaneous nodule and probably homologous with the submiliary cardiac nodule. Coombs [10] has advanced the hypothesis of blood-borne streptococcal infection by showing histologically the manner in which the heart is attacked. In brief his contention is as follows: Streptococci of "parvenu pathogenicity," akin to those normally found in the alimentary tract are disseminated in the blood-stream and develop a special affinity for the cardiac muscle. A specific reaction follows, the stages in which are vascular thrombosis, endothelial response and a new vascular canalization. A fibrotic zone then surrounds the submiliary nodule so formed and the centre of this becomes destructuralized, with the eventual formation of a scar of dense fibrotic tissue. This process spreads by the newly formed vascular tissue, right up to the base of the valve flap, which in its turn becomes canalized, so that if the inflammatory process comes to lie under the free edge of the flap, the endothelial lining at the point of contact with its opposite number is liable to rupture, with the formation of a cap of protective fibrin and thus the basis of a cardiac vegetation is formed. Describing the histology of rheumatic infection, Coombs [11] says "the centre of the lesion is a thrombosis around which is a zone of extraordinarily rich and exuberant proliferation of fibrous and endothelial cells; these last throwing off not only detached uninucleate cells, but also new capillary buds in great numbers, and forming, possibly as an early phase of this budding, the multinucleate cells that are so striking a feature of the rheumatic reaction. These characters, the thrombotic centre and the endothelial periphery, stamp the node as a vascular lesion."



From the *Medical Journal and Record*)

FIG. 1.—RHEUMATIC FEVER.

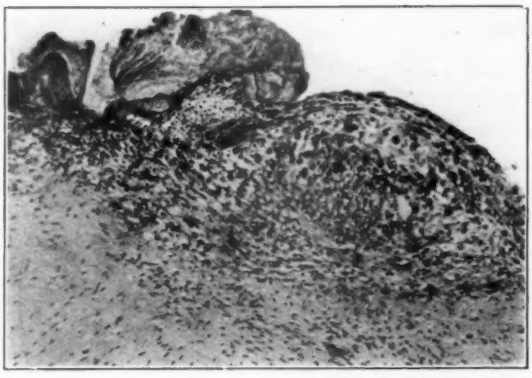
Subcutaneous node. Sections of a relatively large lesion arising during the acute stage of the disease in a child. The lesion is in a fairly early phase. A mass of autolysing fibrin occupies the centre (C). The intermediate zone is composed of inflammatory cells (I); the peripheral zone, of granulation tissue in which at a later stage large numbers of young capillaries arise (P).



(From the *Archives of Disease in Childhood*)

FIG. 2.—RHEUMATIC FEVER.

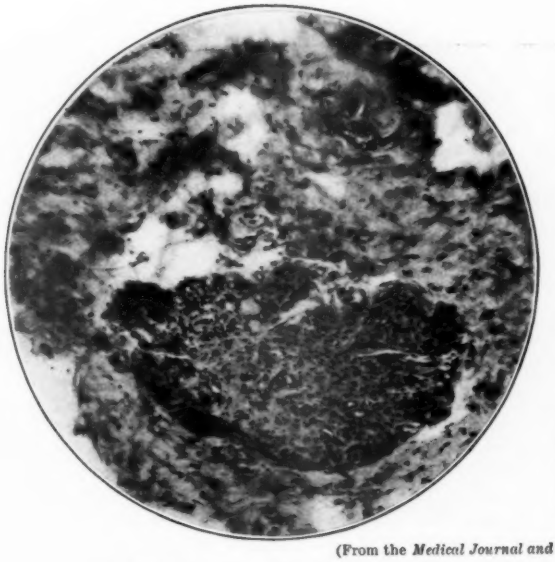
Subcutaneous node. A higher power view of a rheumatic node in its early stages showing exuberant production of new fibrous and vascular tissue.



(From the *Medical Journal and Record*)

FIG. 3.—RHEUMATIC FEVER.

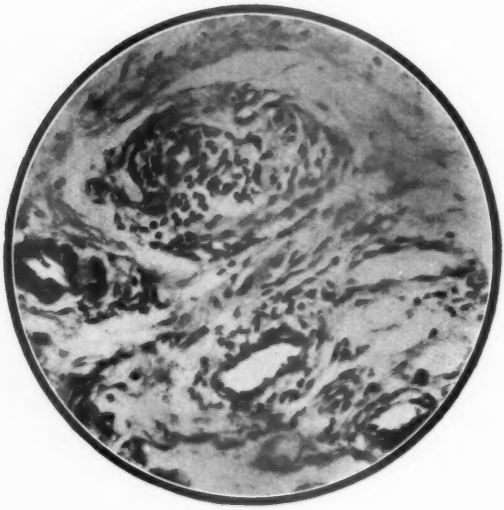
Valvular endocardium. Section of "vegetation" of acute rheumatic endocarditis. A nodule of inflammatory cells lies beneath the valvular endocardium. Its histological characters are essentially those of the nodule found in the myocardium and mural endocardium. At one point the stretched endothelial lining has ruptured and a protective mass of fibrin lies over the rupture.

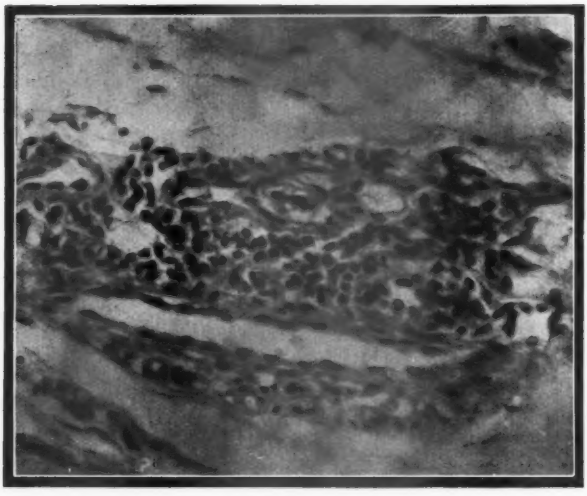


(From the *Medical Journal and Record*)

FIG. 4.—SUBACUTE RHEUMATIC INFECTION.

Millet seed granule. From a child without signs of organic cardiac disease. The lesion, only just palpable, has, in miniature, all the characters of the larger lesions found during the acute phase of frank rheumatic fever. It is sharply circumscribed and is rich in newly formed capillaries.





(From the *Archives of Disease in Childhood*)

FIG. 5.—SUBACUTE RHEUMATIC INFECTION.

Millet seed granule. Higher power. Note the formation of new capillaries.

(2) *The stages by which the conclusion is reached that heterodox rheumatic infection gives a similar tissue reaction to that of orthodox infection.*

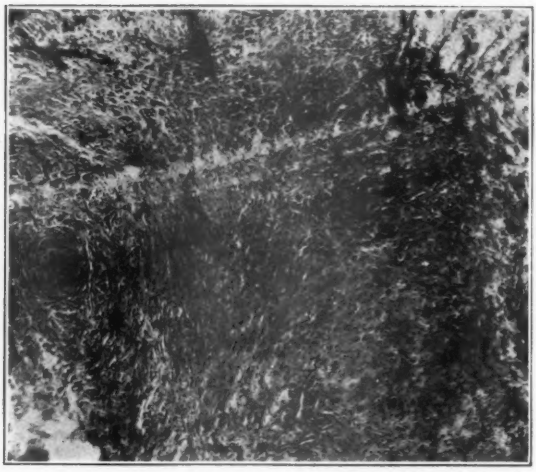
Hawthorne [12] in a particularly well-written monograph stated that "it is to Heberden (1710-1801) and Haygarth (1740-1827) that the responsibility of first endeavouring to advance rheumatoid arthritis to the position of an independent disease must be attached," but as "gout," "osteo-arthritis" and "rheumatic gout" were terms used by the older writers in no very clear way, he set himself to inquire whether or not subcutaneous nodules occurred in heterodox as in orthodox rheumatic disorders. "For if they do so occur, one of two conclusions is inevitable. Either rheumatoid arthritis is rheumatism, or the development of fibrous tumours in the subcutaneous tissue is not a special and distinctive note in rheumatism." He formed an opinion to the effect that these nodules "did occur in a distinct proportion of cases of rheumatoid arthritis non-sequential to acute or subacute articular rheumatism"; that they could not be distinguished from the nodules of orthodox rheumatic infection, but that their mere presence did not prove a rheumatic condition. In 1926 Coates and Coombs [11] examined sections cut from nodules removed from cases of infective arthritis, and considered them histologically identical with those of orthodox rheumatic infection. Coates [13] further noted the presence in infective arthritis of the same millet-seed granules he had previously described in rheumatic children. As a further step sections are here described of a bursa removed from a case of infective arthritis, and Professor Geoffrey Hadfield, to whom we are indebted for the production of every section shown, has written as follows:

> "This bursa shows subacute productive inflammation which is perivascular in distribution and in one or two places there are localized inflammatory nodules, rich in young capillaries and large endothelial or histiocytic cells. These nodules immediately recall those of an acute rheumatism and do not differ from them essentially in structure."

It now remains to discuss the pathology of other subcutaneous nodules which might be mistaken histologically for those of an orthodox or heterodox rheumatic infection.

Syphilis can be dismissed in a word and is only noted because syphilis was suspected or present in some instances of subcutaneous nodules formerly reported. We now know that syphilis evokes its own typical response.

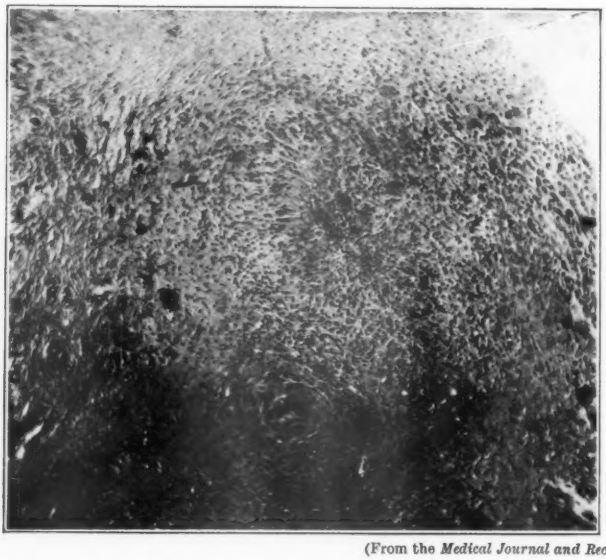
In scleroderma the reaction is essentially fibrous as opposed to the cellular response of rheumatic lesions. The lesions of erythema nodosum bear no resemblance to those of rheumatic infection. The subcutaneous nodules of endocarditis lenta on the other hand, are similar to those under discussion, as has been shown by Coates [11] and Coombs. There is good reason to suppose, however, that endocarditis lenta is a streptococcal disease and, as such, it would in the prevailing opinion fall into line with rheumatic carditis, though its exact relation to orthodox infection is at present doubtful. In respect of subcutaneous nodules in gout, while many of the abarticular subcutaneous lesions are full of bi-urate crystals and are frank tophaceous deposits, yet that type of gout which is apt to masquerade as infective arthritis not uncommonly has subcutaneous nodules true to the rheumatic type. It is not unlikely that this form is what the older writers really meant by "rheumatic gout." The relationship of true gout to orthodox rheumatic infection is not easy to assess correctly, but rheumatic fever occurs in a certain percentage of cases of true gout and clinically gout is not infrequently complicated by infective arthritis or is of such a nature as to defy detection without uric acid estimates or the occurrence of a typical attack. The so-called "nodules," often palpable in the gluteal region of fat women suffering from fibrositis, which give the sensation of



(From the *Medical Journal and Record*)

FIG. 6.—INFECTIVE ARTHRITIS.

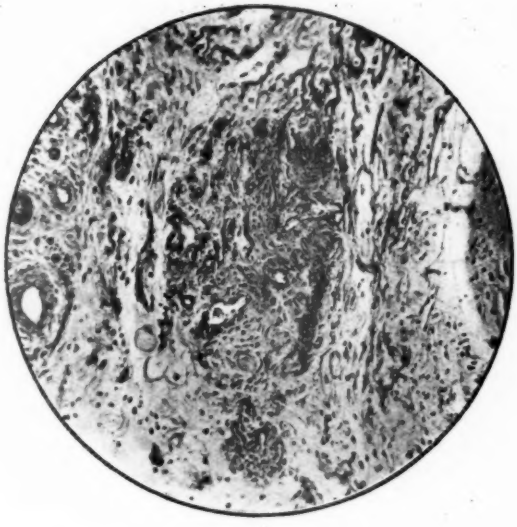
Subcutaneous node from a case of polyarthritis with enlarged spleen and glands and achlorhydria. A central mass of necrotic tissue which has become hyaline, surrounded by a fibrocellular zone.



(From the *Medical Journal and Record*)

FIG. 7.—INFECTIVE ARTHRITIS.

Subcutaneous node from a child with fusiform joints, and enlarged glands and spleen. There is central necrosis with peripheral fibroblastic reaction as in the subacute phase of frank rheumatic fever.



A

B

FIG. 8.—INFECTIVE ARTHRITIS.

A.—Low power. *B*.—High power.

Bursa from a woman aged 63 suffering from moderately severe arthritis of scattered distribution. Note the inflammatory nodule rich in young capillaries and endothelial cells essentially the same in structure as those of acute rheumatic fever.

lying in the gluteal muscles, are in reality, fatty masses surrounded by a fibrous envelope in the subcutaneous tissues. This can be verified by transfixion and surgical exposure.

REFERENCES.

[1] COATES, VINCENT, *Brit. Med. Journ.* 1930 (i), 67. [2] In Davaine, J. A., "Contribution à l'étude du rhumatisme," Paris, 1879. [3] In Jaccoud, S., "Traité de Path. Int.," Paris, 1871, ii, 546. [4] BARLOW, T., and WARNER, F., *Trans. Fourth Internat. Med. Congress*, London, 1881, 116-118. [5] GEIPEL, P., *Deutsch. Archiv für klinische Medizin*, Leipzig, 1905, lxxxv, 75. [6] ASCHOFF, L., and TAWARA, S., *Brit. Med. Journ.*, 1906 (ii), 1103. [7] POYNTON, F. J., and STILL, G. F., *Trans. Path. Soc.*, London, 1899, 50, 324. [8] COOMBS, CAREY, *Journ. Path. and Bact.*, 1911, xv, 489. [9] COATES, VINCENT, *Brit. Med. Journ.*, 1925 (i), 550. [10] COOMBS, CAREY, "Rheumatic Heart Disease," 1924. [11] COATES, VINCENT, and COOMBS, CAREY, *Arch. Dis. Childhood*, 1926, 183. [12] HAWTHORNE, C. O., "Rheumatism, Rheumatoid Arthritis, and Subcutaneous Nodules," 1900. [13] COATES, VINCENT, Bath Conference, 1925, *Trans.*, 181.

Clinical Section.

[*February* 14, 1930.]

Anal Polyp and von Recklinghausen's Disease.—PHILIP TURNER, M.S. E. T., female, aged 54, admitted to hospital on account of a rectal polyp, causing great pain and difficulty on defæcation. The polyp had been present for many years, but recently there had been considerable difficulty in replacing it after protrusion. On admission, the polyp, which was about 3 in. in diameter, was strangulated and was partly necrotic. For many years patient has had large numbers of soft, painless, subcutaneous tumours, varying in size from that of a pea to that of a hen's egg, and, with the exception of the anal tumour, have never caused her any trouble. Also complains of "rheumatic" pains in left leg. X-ray examination showed multiple areas of chronic periostitis in the left tibia with no under-lying central foci. Several other bones were examined but no changes were seen. Wassermann reaction negative. The anal polyp, which was the size and shape of a small pear, was removed and a tumour from the upper lip was also excised. Histological examination showed the latter to be a non-cellular fibroma, while the former, though extremely necrotic, showed many disintegrated lymph follicles and appeared to be a lymphoma.

Discussion.—Dr. J. W. CARR (President) asked what relationship existed between the bone changes in the tibia and fibula and the other conditions present.

Dr. F. PARKES WEBER said he believed that in Mr. Turner's case the anal polyp was almost certainly of the same neurofibromatous nature as the numerous superficial molluscous fibromata with which the patient's body was covered. He further suggested that the periosteal changes in the left tibia and fibula were of the nature not of chronic periostitis, but of true periosteal neurofibromatosis, that, in fact, they constituted a lesser degree of the remarkable periosteal neurofibromatosis recently described and illustrated by Dr. Perdrau and himself,[1] in the case of a woman, aged 47, whose body presented the characteristic pigmentation and multiple molluscous fibromata of Recklinghausen's disease. In that case there were likewise small intestinal neurofibromata (on the peritoneal surface of the ileum), and microscopic sections from a molluscous tumour of the skin, the periosteal mass, and one of the little intestinal growths, showed exactly the same histology, proving them to be all of neurofibromatous nature.

Fracture of the Cervical Spine.—CECIL P. G. WAKELEY, F.R.C.S.

S. K., male, aged 17, fell off the parallel bars in a gymnasium on to his shoulder. He immediately lost the use of his legs, but this returned just before an ambulance came to take him to hospital.

On admission to hospital, June 14, 1929, it was found that he could move his legs, but complained of numbness and weakness in them. There was a hæmatoma situated over the vertebra prominens. A skiagram of the cervical spine was taken, but no fracture was seen. The boy was kept in bed. Abdominal reflexes absent, but knee-jerks brisk. He remained *in statu quo* until June 21, 1929, exactly a week after his accident, when he lost the use of both legs and complained of pains in both arms. The pupils were unequal, left > right. All reflexes very brisk, excep abdominal, which were absent. Extensor plantar response on both sides. Abdomen was distended. The intercostal muscles were not working. There was definite sweating on the face, but none on the abdomen. There was complete anæsthesia below the fifth rib. He was seen by my colleague, Dr. Macdonald Critchley, who agreed that laminectomy should be performed forthwith. The cervical spine was explored the same day under intratracheal anæsthesia. The cervical

[1] F. Parkes Weber and J. R. Perdrau, "Periosteal Neurofibromatosis, with a short consideration of the whole subject of Neurofibromatosis," *Quart. Journ. Med.*, Oxford, 1930, xxiii, 151-165.

spines from the third to the seventh, were removed, and the laminæ exposed. A fracture of the fifth cervical vertebra was seen. The laminæ of the fourth, fifth, and sixth cervical vertebræ were removed, and a large flattened extradural clot was exposed (see figure.) There was no pulsation of the spinal cord. The clot, which was an elongated one extending up to the level of the fifth cervical root, was removed in one piece. Pulsation of the cord returned immediately. There did not seem to be any thickening of the dura. The wound was closed and a dressing applied.

The next day the patient could move his legs, and the plantar reflexes were flexor. Sensation had returned to the trunk and legs. Pupils were equal. Blood-pressure 138/100. Both grips were poor.

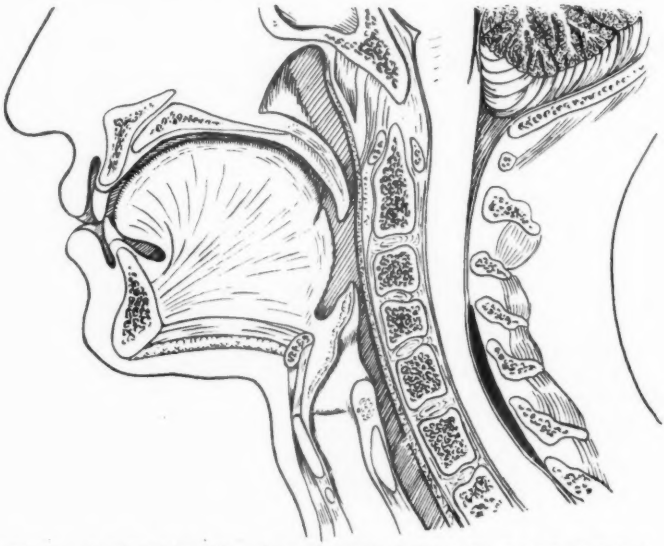


Diagram showing the position of extradural blood-clot. (Mr. C. P. G. Wakeley's case of fracture of the cervical spine.)

On June 24, 1929, patient complained of tingling in both hands. Grips were better, but did not improve as rapidly as was expected, and the extensor muscles of the arms were weak. It was thought possible that there might have been a small intradural hæmorrhage, so a second operation was performed July 5, 1929. The previous incision was re-opened and the dura mater explored. On opening the dura mater the cerebrospinal fluid squirted out under considerable pressure, and was quite clear. There was no evidence of any hæmorrhage within the dura, and the cord was pulsating in a normal manner. The dura was sutured and the wound closed.

The grips began to improve gradually, and massage to the arms was given. Patient was discharged from hospital September 24, 1929. At present he has definite weakness of the intrinsic muscles of his hands, and some weakness of the neck muscles.

Discussion.—Dr. NEILL HOBHOUSE said that much could be learned from the distribution of the residual paralysis in this case. It was striking that the paralysis the patient now had was in the area of the nerve-roots which were not involved in the operation; it was in the muscles supplied by the eighth particularly, and to some extent by the first thoracic. He wondered whether the clot itself extended to the level of the fifth cervical root or whether it was simply that the segments which were cleared at the operation recovered, and those just below it did not.

Dr. W. M. FELDMAN asked whether any explanation could be offered as to the persistence of absence of the abdominal reflexes as well as of the exaggerated knee-jerks, considering that the blood-clot was removed, and there was no injury to the spinal cord.

Mr. WAKELEY (in reply) said that Dr. Neill Hobhouse had raised an interesting point; it was difficult to be sure whether there was any injury to the roots, or whether the blood-supply to the roots had been cut off, probably owing to fibrous tissue formation.

He had no explanation to suggest as to the absence of the abdominal reflexes.

Dislocated Carpal Semilunar Bone.—CECIL P. G. WAKELEY, F.R.C.S.

B. O'F., aged 29, a builder, was standing on the lowest tread of a ladder, and turning round to speak to a man, he slipped and fell on to his outstretched right hand. The hand became swollen and he was unable to use it, so he went to see his doctor the day after the accident. The hand was treated with a lotion and the patient was sent up to hospital to be radiographed.

The skiagram revealed a dislocated semilunar bone (fig. 1) and a fracture of the styloid process of the radius. There was definite numbness over the distal distribution of the median nerve, and continual "pins and needles" in the thumb and outer two and a half fingers.

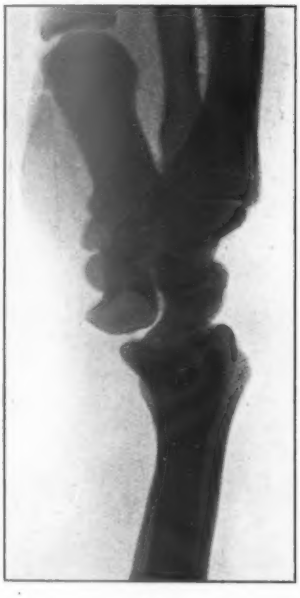


FIG. 1.

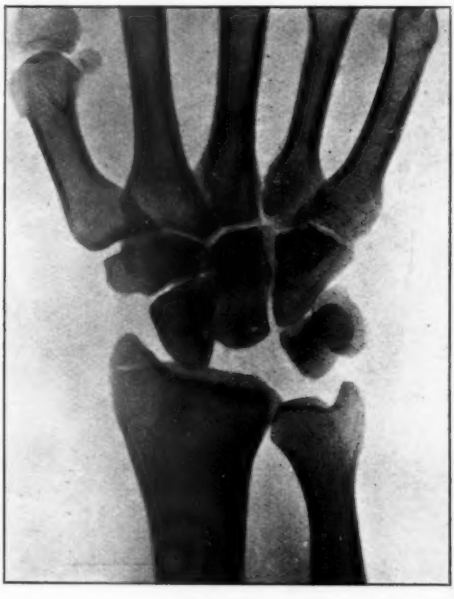


FIG. 2.

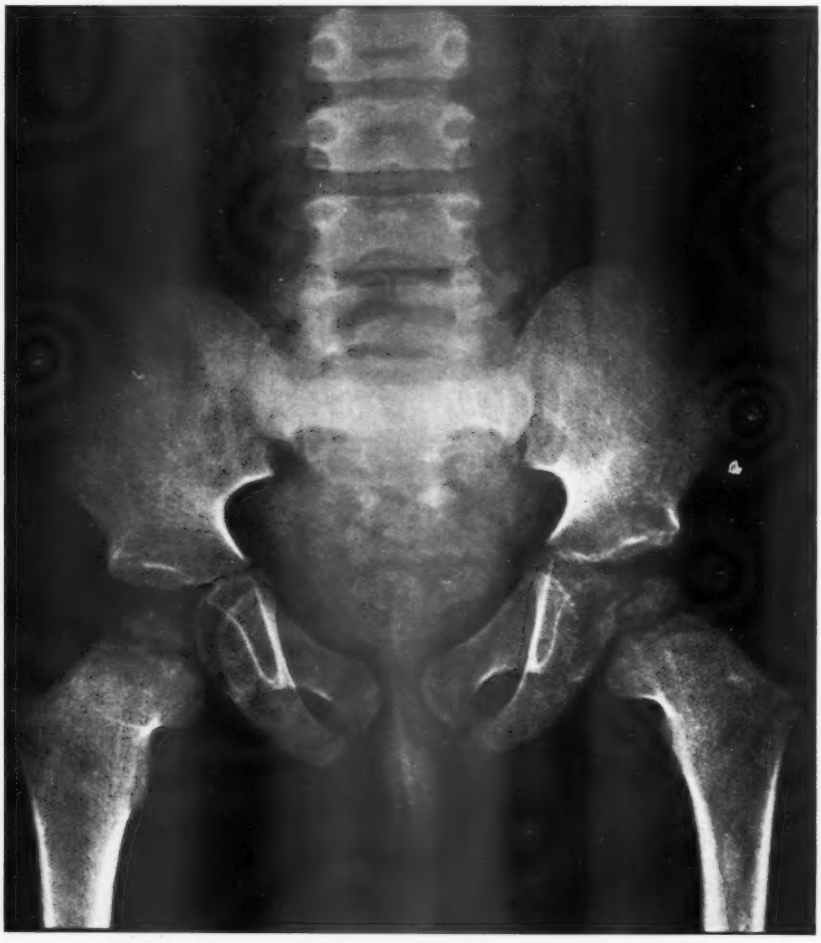
FIG. 1.—Lateral skiagram showing dislocated semilunar bone.
FIG. 2.—Antero-posterior skiagram after removal of the semilunar bone

January 23, 1930.—Excision of the semilunar bone was performed through a short vertical incision just proximal to the wrist-joint. The median nerve was exposed and retracted. The dislocated bone was seen beneath it and easily removed. The wound was closed and the hand placed on a "cock-up" splint. The numbness of the hand disappeared on the day following the operation. Fig. 2 shows the condition of the carpal bones following the removal of the semilunar.

It is very uncommon to see a case of isolated displacement of the semilunar without luxation or fracture of the scaphoid, in fact, Dr. Etienne Destot,[1] of of Lyons, goes so far as to say that it never occurs.

Köhler's Disease, with "Mulberry" Upper Femoral Epiphyses.—CECIL P. G. WAKELEY, F.R.C.S.

This boy, aged 5, first came under observation in January, 1929, because his mother noticed that he had a limp. On examination nothing was found to account for the limp. There is a typical bilateral tarsal scaphoiditis which is clearly demonstrated in the skiagrams of the feet. Movements of hip-joints were full and



Skiagram by Kodak, Ltd., showing "mulberry" upper femoral epiphyses.
(Mr. Wakeley's case of Köhler's disease.)

1 Destot, Etienne, "Injuries of the Wrist," 1925.

free; the back was quite straight. X-ray examination revealed curious flattened "mulberry" upper femoral epiphyses (see figure). The pelvis is somewhat deformed and in the sacrum there is a deficiency in the laminæ. The rest of the skeleton has been examined by X-rays and except for upper humeral epiphyses, appears normal. The knee-joints are expanded, but do not show any changes due to rickets.

The child has been in hospital for the last month for a thorough examination. He appears somewhat stunted; knees slightly broadened and face flattened; is very intelligent for his age and talkative.

All joints quite supple, and no evidence of any rheumatic lesion. Wassermann reaction negative. Blood-count January 13, 1930: Red cells 4,320,000 per c.mm. (86% of normal); no abnormal forms seen. Hæmoglobin 84%, colour-index 0·98. White cells 8,000 per c.mm. (*Differential*: Polymorphonuclears 61%, eosinophils 4%, basophils 0·4%, lymphocytes 34·5).

Urine normal; specific gravity 1001. Blood-urea 29 mgm. per 100 c.c. Blood calcium 10·4 mgm. per 100 c.c.

The boy has a younger brother aged 2½. Family history negative.

The case at first sight was thought to be one of bilateral pseudocoxalgia, but differs from that condition in the X-ray appearances of the upper femoral epiphyses.

Large Painless Tuberculous Ulcer of the Tongue. — CECIL P. G. WAKELEY, F.R.C.S.

The patient, a man, aged 35, was sent to a sanatorium in 1927 with pulmonary tuberculosis of the right apex. While there he accidentally broke a clinical thermometer in his mouth one morning when his temperature was being taken. A small wound was produced on the underside of the right half of the tongue. This soon became a small ulcer and has never healed, but has gradually been getting larger. It is an irregular ulcer measuring ¾ in. by ½ in., and the edges are undermined: it is quite painless. There is extensive involvement of both lungs and tuberculous laryngitis. This is the third case of painless tuberculous ulcer of the tongue which has been shown before the Section this session.

Dr. PHILIP ELLMAN said he was particularly interested in this case as the patient had actually been under his care in the sanatorium in 1927 at the time when he broke the thermometer. He (Dr. Ellman) had seen a number of these cases which, in his experience, had always occurred following some slight injury to the tongue. In the cases he had seen the ulcers, had been painful, and on questioning this patient closely it would be found that he was careful not to allow any food to come into contact with the ulcer, and no doubt this was why he had no real pain. Another point of unusual interest was the fact that although the ulcer was of fairly long standing, the tuberculous laryngitis was of comparatively recent onset.

Splenomegaly: Case for Diagnosis.—TERENCE EAST, M.D.

Female, aged 29. Married, two children.

Past History.—For some years attacks of pain in right hypochondrium. Five years ago an attack of jaundice lasting some months, during which the stools were clay-coloured. June, 1929.—Jaundice, with bile-salts in urine, but no pigments. November, 1929.—A long thickened appendix removed: considerable thickening around right kidney. January, 1930.—Still complaining of pains in right side. There was definite jaundice. The urine contained bile-salts, since absent, for several days, but no pigments. The spleen was considerably enlarged, the liver was palpable but not abnormal to the touch. There were several purpuric blotches on the legs. Fæces normal in colour. Investigations giving the following results have been carried out:—

Fragility of red corpuscles (January 20, 1930) slightly less than usual. Wassermann reaction negative.

Lævulose tolerance test (January 22, 1930), suggests slight liver defect. Coagulation time (January 15, 1930), normal.

Blood-counts, and van den Bergh Test.—A fairly constant anæmia of secondary type, no abnormality being present in the white cells or the form of the red cells.

	R.B.C.'s Percentage	Hb Percentage	Platelets Percentage
January 15, 1930 ...	71	58	28
,, 24, ,, ...	63	—	18
February 5, ,, ...	77	62	23

Van den Bergh test.—January 16, 1930: Delayed, 1·5 units (normal 0·2 – 0·6). January 31: Biphasic; definite trace of "prompt reaction" pigment, 1·0 unit. February 5: delayed, 0·72.

The salient features thus are: (1) Splenomegaly, associated with thrombocytopenia and purpura; (2) defect of liver, associated with non-obstructive jaundice and bile-salts in urine; (3) secondary anæmia.

I ask what treatment Members would recommend. Ought the spleen to be removed? Would this prevent the development of further grave defect in the liver? She is improving, but in a few months' time the whole cycle may be repeated.

Discussion.—Dr. BERNARD MYERS said that the capillary resistance test should be made in this case. Some of the worst cases of thrombocytopenia hæmorrhagica had no enlargement of the spleen; sometimes the spleen was slightly enlarged, but usually became normal in size again in a week or two. If in this case the spleen were removed he did not think the operation would do harm, and it might cure the condition and prevent future trouble.

Dr. H. S. STANNUS said that a definite mass could be felt in the right iliac fossa. There was said to have been a thickening around the right kidney at the time of the appendix operation, and he asked what that thickening was due to and whether it was the mass which could be felt.

Dr. EAST, in reply, said he thought enlargement of the spleen had existed longer than the history indicated. He would keep the patient under observation for a longer period, and should symptoms increase, he would have the spleen removed.

Two Cases of Essential Thrombocytopenic Purpura Hæmorrhagica[1].—BERNARD MYERS, C.M.G., M.D.

(I) Mrs. D., aged 32, has been shown before this Section annually for five years. Previously suffered from essential thrombocytopenic purpura hæmorrhagica, the chief symptom of which was uncontrollable menorrhagia. Splenectomy four years ago; no sign of purpura since then.

Blood-count at present: Red cells 4,480,000, hæmoglobin 81%, colour index 0·9. White cells 8,220, polys 68·5%, lymphocytes 22·5%. Red cells microscopically normal. Platelets 201,000 per c.mm. Capillary resistance test negative after three minutes. Bleeding time 3 minutes 15 seconds.

The patient now enjoys perfect health.

(II) W. B., a girl, aged 14, has been shown before this Section annually for five years. Originally in hospital on account of essential thrombocytopenic purpura hæmorrhagica, the main symptom being uncontrollable bleeding from the mouth. Splenectomy four years and three months ago. In perfect health since.

Red cells 4,100,000, hæmoglobin 72%, colour index 0·88, white cells 6,200, polys 36%, lymphocytes 41%. Red cells show slight anisocytosis but are otherwise normal in appearance. Platelets 120,000 per c.mm.

1 See *Proceedings*, 1922, xvi (Clin. Sect.), 10; 1925, xviii (Clin. Sect.), 19; 1926, xix (Clin. Sect.), 31, 37; 1927, xx, 541 (Clin. Sect. 30), 1190 (Clin. Sect. 33); 1928, xxi, 757 (Clin. Sect. 69); 1929, xxii, 755 (Clin. Sect. 49).

Purpura.—BERNARD MYERS, C.M.G., M.D.

Mrs. A. B., aged 45. Has had five children and three miscarriages. Admitted to hospital October 29, 1929, with purpuric spots on the chin, which had occurred intermittently for three years. Had hæmaturia three times; no vaginal hæmorrhages; no epistaxis or hæmoptysis. Purpuric spots present on face, chest and abdomen. While in hospital had ecchymoses on both eyelids. Group protein tests all negative. Blood calcium, 6·3 mgm. per 100 c.c. Parathyroid given gr. $\frac{1}{10}$, with calcium lactate gr. 4, which greatly improved her. Re-admitted to hospital three weeks after discharge, with enormously swollen lower lip, which was distinctly discoloured and fissured, with some pus oozing out. Many purpuric spots on the chin and also in the mouth, but none of the latter was actually bleeding. Large swelling in left cheek, ? angio-neurotic œdema; another swelling appeared below mandible, which increased daily, and from which over half a pint of pus was evacuated. On examination, pus contained *Streptococcus hæmolyticus*. Transfusion performed and 600 c.c. of blood given. Marked constipation present, and meteorism appeared in abdomen; given 0·5 c.c. pituitrin and enemas twice daily. Mouth treated with a sodium bicarbonate and carbolic lotion which kept it fairly clean. Distinct pain in right flank with impaired note, ? angio-neurotic œdema or pus, but subsequent events proved it was not the latter. 20 c.c. *B. welchii* serum given intramuscularly with no improvement; much local reaction. Lately there have been profuse hæmaturia and œdema of the leg. At present there is fluid in the abdomen. Capillary resistance test negative. Bleeding time normal. Blood-counts show no special abnormality. The platelets varying from 285,000 to 165,000, but at present not over 200,000. No apparent increase in coagulation time.

Knyvett Gordon made platelet counts and found the number to be 300,000 when patient first came in; marked purpuric spots were then made with the finger on the chest, and, fifteen minutes later, platelets were estimated again, and were once more 300,000. The question is as to actual cause of purpura on various occasions, the urine showed albumin and red blood-cells. Hyaline casts were present and some renal tubules. Wassermann reaction negative. Fæces negative. Blood-culture sterile on three occasions.

I suggest that this is a case of Henoch's purpura in an adult.

Spina Bifida (two other cases in same family).—BERNARD MYERS, C.M.G., M.D.

H. G., aged 9 weeks. Suffers from meningo-myelocele in lumbo-sacral region. Four in family, including girl twins (died first week), both of whom had spina bifida. No other case in family. Wassermann reaction negative. Sac does not leak. Circumference of head steadily increasing during last five weeks, anterior fontanelle being now 2 in. across. Mr. St. J. D. Buxton does not advise operation.

Sir John Bland-Sutton informs me that he has never known so many cases in one family. Bernard Alpers in the *Archives of Neurology and Psychiatry*, 1929, describes a family of ten children, in which six of the nine who were examined had spina bifida occulta—four of these suffered from Friedreich's disease and another showed early symptoms, but the sixth case showed no other abnormality.

X-ray examination of the spine with inflation of the sac with oxygen, as suggested by Sir Robert Jones, could not be carried out in this case, but four lower lumbar vertebræ and upper part of sacrum were shown by X-rays to be involved.

Dr. E. A. COCKAYNE said he would certainly recommend that no operation should be done; if it were, severe hydrocephalus was most likely to occur.

Unusual Case of Loose Body in each Knee-joint, of Traumatic Origin.—PAUL BERNARD ROTH, F.R.C.S.

H. H., a shoeing-smith, aged 30, seen October 30, 1924, with the history that two months earlier he had been shoeing the hind hoof of a horse, when it suddenly pulled back while he was stooping, and caused him to over-extend his right knee violently. It was extremely painful for two or three minutes, and he hardly knew how to bear it; then the pain eased off, and he went on with his work. Next day the knee was twice the size of the other and very painful, but he went to work and remained at work until three weeks before examination, when, in turning round sharply, the knee gave way and became bent, and remained so for two or three days. He could feel something loose under the skin on the outer side, which he could move about.

At operation, performed through the mid-patellar route, a slice of articular cartilage and bone, the size of a shilling, was found almost completely detached from the outer and lower aspect of the mesial condyle, together with a much smaller piece free and loose in the joint. The large piece was only hanging on by a shred at one point. The cavity in the condyle, from which the pieces had come, was healed over in its whole extent with a thin bluish-white film. The loose pieces were removed, and the patient made a complete recovery.

On October 31, 1929, that is, five years later, this patient presented himself at hospital and announced that he had done exactly the same to the *left* knee. He had been shoeing a horse, and it had pulled back in the same way, causing him intense pain in that knee, and now it was impossible for him to straighten it. A skiagram showed a large detached portion of bone free in the joint, beneath the patella, and an irregularity in the outline of the mesial condyle, showing where it had been fractured off. At operation, a large loose body $1\frac{1}{8}$ in. by 1 in. by $\frac{1}{4}$ in. was found beneath the patella: and on the lower aspect of the mesial condyle, just as in the other knee five years before, was the cavity from which it had come, lined with smooth bluish-white tissue. The loose body was removed and the wound closed.

Mr. CECIL WAKELEY said he believed it was the common teaching that trauma played an important part in the causation of loose bodies in joints, especially in the knee-joint. Minute fragments of articular cartilage were torn off, or even portions of synovial fringes became nipped between the bones and detached, and afterwards produced loose bodies.

The operation of splitting the patella was, in his opinion, a dangerous one to advocate as a universal operation for exposing the joint. He had followed up some of the cases in which it had been performed on account of loose bodies and displaced semilunar cartilages. In a considerable number the loose bodies had recurred after an interval.

Facial Lipodystrophia with Unerupted Upper Central Incisor Teeth.—F. PARKES WEBER, M.D., and O. B. BODE, M.D.

D. P., female, aged 8 years and 10 months, has the typical "skin-and-bone" facies of so-called lipodystrophia progressiva. To a lesser degree there is deficiency of subcutaneous fat over upper front of thorax and shoulders, whilst the abdomen and especially the gluteal regions and thighs are at least normally fat and in contrast with the face (see fig. 1). The upper central incisor teeth have not yet erupted; the unerupted teeth can be seen in a skiagram. Abdominal and thoracic viscera normal: no signs of tuberculosis in lungs or elsewhere. Blood-count (January 18, 1930); Hæmoglobin 79 per cent., erythrocytes 4,620,000, leucocytes 6,750 (eosinophils 8%, polymorphonuclears 44%, lymphocytes 40%, monocytes 7%, plasma cells 1%). The Wassermann and Meinicke reactions are negative.

Patient is one of five children. Family history, nothing abnormal. Nothing unusual was observed until the wasted appearance of the face was first noticed at $4\frac{1}{2}$ years. This gradually increased during the following half-year, but has not

become more marked since then. In other respects general physical and mental development has been considered good. With the exception of measles and whooping-cough there have been no serious illnesses—in particular, no affections of the throat or ears, or severe colds; no mental or physical "shocks" of any kind. For figure 1 we are indebted to Dr. M. Scholtz. Figure 2 shows the child at the age of 4 years, before the lipodystrophia had commenced.

Discussion.—Dr. PARKES WEBER said he believed that so-called "lipodystrophia progressiva"—which was by no means always progressive—was best classified with the "congenital-developmental dystrophies," including the primary muscular dystrophies and the various congenital-developmental diseases of the nervous system. Nevertheless, the absence of evidence of familial incidence was rather remarkable. In the present case, as usual, the patient had been treated elsewhere for "debility" (e.g., by cod-liver oil), but, as in nearly all other cases there was no debility (either physical or mental) present.

FIG. 1.

FIG. 2.

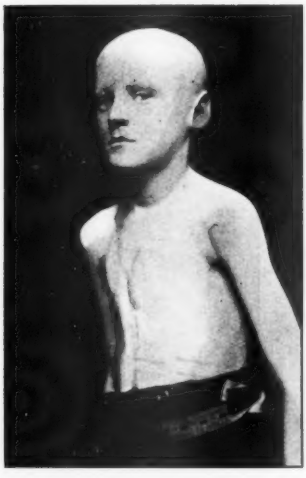
The PRESIDENT said he had noticed that there was a good deal of wasting about the chest and upper part of the body, but the mother assured him that there had been definite improvement in that respect; if that were so he would like to know if Dr. Parkes Weber thought there was any chance of improvement in the facial condition also.

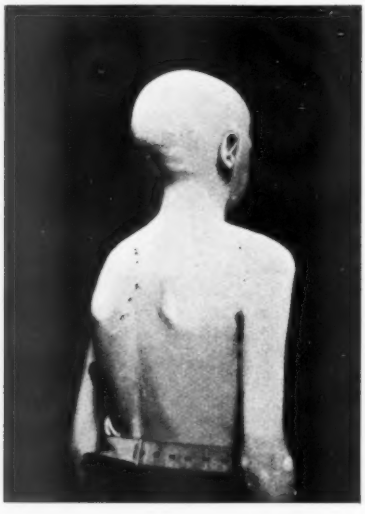
Dr. PARKES WEBER (in reply) said that in only one case had he heard of improvement, and even that was doubtful. Increase in body-weight from excessive feeding and cod-liver oil was due to the accumulation of fat in the thighs and gluteal regions, where it was not required. Apart from the absence of subcutaneous fat in the affected parts, general development (including that of the mammæ) proceeded normally. Intelligence was usually quite up to the average, but the emaciated appearance of the face was a hindrance in obtaining employment.

Alopecia Totalis after Slight Nervous Shock.—F. PARKES WEBER, M.D., and O. B. BODE, M.D.

L. K., male, aged 11¼ years, fair complexion, is completely destitute of scalp-hair, eyebrow hair and eyelashes (see figures), having no hair at all, excepting a little "lanugo" on the right side of his face and about both knees. Otherwise he appears normally developed and free from disease and is satisfactory at school-work. He sweats normally. The tonsils are perhaps slightly enlarged. The thyroid gland appears of normal size. The complete loss of hair occurred within three weeks after his younger brother had to be removed to a fever hospital, in March, 1926, on account of scarlet fever. In June, 1929, scalp-hair, eyebrow-hair and eyelashes reappeared after a sunny holiday at the seaside, but this fresh crop was again lost a few weeks after his return to London—in spite of treatment at a "sunlight clinic."

Past History.—Patient was born at the eighth month; nothing remarkable about his hair until at the age of 3 years he temporarily lost some from the lower





part of the scalp after measles with broncho-pneumonia. At 5 years of age he developed bald patches on his head after a scalp-wound (knocked down by a bicycle), but the hair grew again in the course of a few months. His twin sister is quite normal, and there is nothing of importance in the family history, excepting that his father (now aged 43 years) developed baldness of the top of his head (of the ordinary "seborrhœic type") rather early (when about 30 years of age).

Discussion.—Dr. PARKES WEBER said that he was inclined to regard this case as a *delayed* ectodermal defect,[1] "potentially" congenital. The pilous system in such a case was apparently normal at first, but a mental shock or the toxæmia of an infectious disease was sufficient to produce partial or complete baldness. If no recovery took place the case might be regarded as a "retrogressive dystrophy," allied to the "abiotrophies" of Sir William Gowers.

[1] Cf. F. Parkes Weber, "A Note on Combined Congenital Ectodermal Defects," *Brit. Journ. Child. Dis.*, 1929, xxvi, 270.

In reply to a question by the President he agreed that the general health was the most important point, and this child should be brought up in the country, if possible, with plenty of open air and sun.

Fracture of the Neck of the Femur through a Solitary Cyst in the Bone.—HAROLD EDWARDS, M.S.

Spontaneous fracture through the neck of the femur occurred nearly five and a half years ago, when the patient was 6 years old.

History.—Boy, now aged 11½ years, only child of moderately healthy parents. Birth weight 9 lb.; instruments used at delivery; bottle fed; always a weakly child.

In March, 1924, he had a severe attack of measles, complicated by acute mastoiditis, for which an operation was performed in the following June. Immediately after this, chickenpox developed, and he was finally discharged from hospital on October 17, 1925.

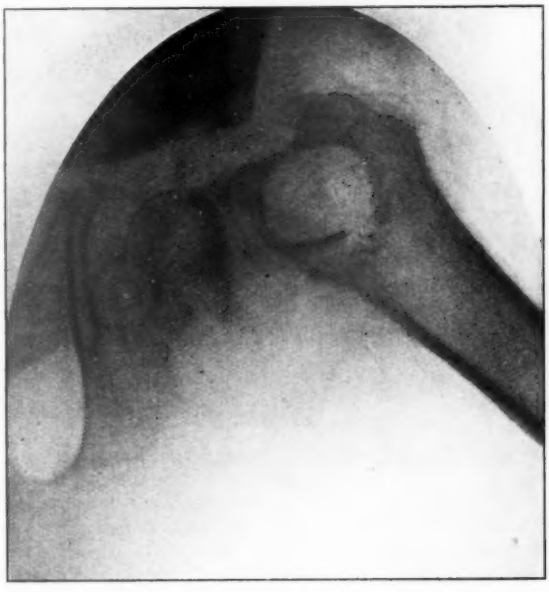


FIG. 1.—X-ray appearances two months after fracture. (Mr. Harold Edwards's case of fracture of the femur through a cyst.)

Exactly one week later he appeared to twist and crumple up when crossing the road. He was picked up and taken home. He complained of pain in the left hip, and was admitted to King's College Hospital later the same day.

A skiagram showed a well-defined oval clearance in the neck of the femur, with a fracture running through it (fig. 1).

The limb was put up in a Thomas splint in abduction, with a weight extension. This was replaced, after three weeks, by a double long Liston splint, with a hinge opposite the affected joint, so that the limb could be held in full abduction.

The splint remained on for ten weeks, and after a further period of recumbency the patient was allowed to walk with a caliper.

The cyst slowly became obliterated by bone, and at the end of the second year could hardly be made out in a skiagram. In the most recent skiagram it is seen to have entirely disappeared, and to have been replaced by an area of bone rather denser than that surrounding it.

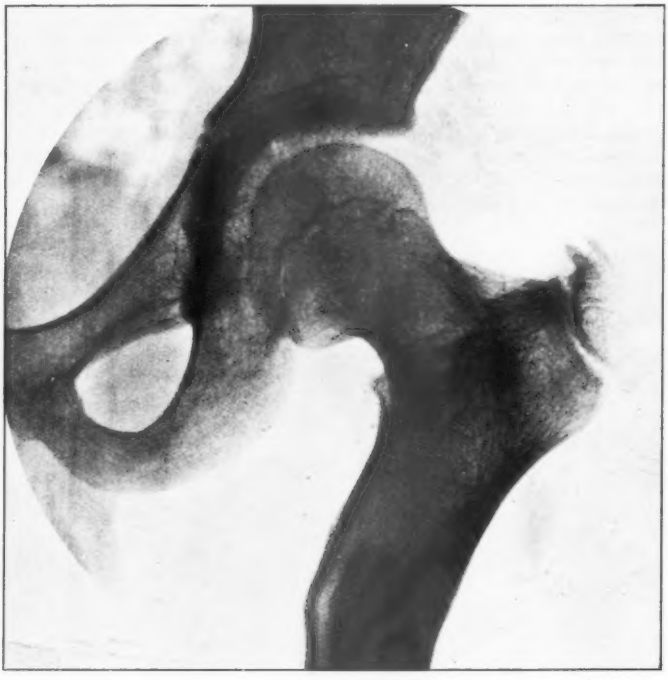


FIG. 2.—X-ray appearances five years after fracture. (Mr. Edwards's case.)

The fracture resulted in a coxa vara, for which osteotomy was performed in July, 1927, nearly three years after injury.

Present measurements: Actual shortening, $1\frac{1}{4}$ in., apparent shortening, $\frac{1}{4}$ in.

The report of other cases shown at this meeting will be published in the next number of the "PROCEEDINGS."

Section of Comparative Medicine.

President—Captain S. R. DOUGLAS, F.R.S., I.M.S.(ret.).

[*October* 23, 1929.]

PRESIDENT'S ADDRESS.

Some Recent Researches on Virus Diseases.

By S. R. DOUGLAS, F.R.S.

VIRUS diseases are so common in man and animals that they cannot fail to be of equal interest to human and veterinary practitioners. I therefore propose to bring before your notice certain of the more recent researches on these diseases. As there is not time to deal with all the recent work, I have chosen largely those researches with which I am best acquainted, although there are many of equal merit which will not be mentioned.

Since it is of more practical interest, I shall commence with an account of the work that has given rise to practical results. I refer to those researches which have led to the production of an "active" immunity against the disease in question, and in this field much has been accomplished in the last few years.

Foot-and-Mouth Disease.—Vallée, Carré and Rinjard (1925) found that cattle injected subcutaneously with an emulsion of the mouth lesions of infected cattle inactivated with formalin, showed no symptoms when injected subsequently with active virus. These authors state that it is important that the tissues—in these experiments the epithelium covering early mouth lesions—used in the preparation of the vaccine, should contain a high concentration of the virus. The workers at the Lister Institute (Maitland, Bedson and Bunbury), employing guinea-pigs instead of cattle, confirmed the work of Vallée, but they found that the immunity produced was not absolute since, although guinea-pigs resisted intramuscular injection of active virus and showed no recognizable symptoms, active virus injected into the pads of the hind foot produced a local lesion with proliferation of the virus locally. This, however, was not followed by generalization of the disease with lesions appearing in the tongue and other feet, which is almost constant in unvaccinated animals. Later, Vallée and his co-workers (1928) have prepared a vaccine from infected guinea-pigs, using practically the whole animal emulsified in a solution containing formaldehyde, and have claimed that the subcutaneous injection of this vaccine into cattle produces a solid immunity.

Unfortunately, at least three strains of foot-and-mouth disease virus exist, and a vaccine prepared from one strain produces immunity against that only, leaving the animal fully susceptible to other strains. The immunity produced even after an attack of the disease, is apparently short-lived in comparison with many other virus diseases. In consequence, no field experiments have been made, and active immunity in foot-and-mouth disease has at present no practical application, especially in this country.

Fowl Plague.—Passing now to fowl plague, Todd (1928), after repeating earlier work without any success, found that an emulsion of virulent liver, treated with 0·02 per cent. solution of formalin did not give a solid immunity, even when three massive doses were given, although this process inactivated the virus. However, this procedure appeared to give some degree of resistance as the vaccinated birds lived very much longer than those which had no treatment.

Continuing his researches, he next prepared a vaccine from a virulent liver, but, instead of emulsifying in a solution of formalin, he employed one containing 60 per cent. glycerine and 0·5 per cent. phenol. Such an emulsion became inactivated in four or five days at 20° C., but was usually kept at this temperature for seven days,

after which it was stored in a cold room at − 3° C. Fowls inoculated with three doses of this vaccine were found, on testing with many thousand infective doses of active virus, to be quite immune.

One other point in Todd's work is worth noting, although at present no explanation can be given for it. This is, that if an emulsion of washed blood-cells, containing the great majority of the virus present in the blood, is treated with a similar carbol-glycerine solution to that used in the preparation of vaccine made from the liver, no inactivation of the virus takes place, even after fifty-three days at room temperature.

Rabies.—As early as 1921 Umeno and Doi, stimulated by the work of Fermi, introduced a preventive vaccine for use in dogs against rabies. This consists of an emulsion of the brain and cord of a rabbit dead from rabies, emulsified in a carbol-glycerine solution. One large dose divided into two portions and given at different sites is recommended. Of late years this method has been widely adopted, not only in Japan and other parts of Asia, but also in Europe and America. The results obtained have been excellent.

Distemper in Dogs and Ferrets.—In 1928 Laidlaw and Dunkin published an account of their work on this subject which had been in progress for several years. They found that an equally efficient vaccine could be made by treating a spleen emulsion with a solution containing either phenol or formaldehyde, but that the latter was preferable on account of the toxicity of phenol for the dog. Spleen emulsion inactivated by heat also produced immunity when large doses were given. A temperature of 55° C. for 1 hour, or 60° C. for 30 minutes, was necessary to inactivate the virus. Only spleens containing a very high concentration of virus produced an efficient vaccine. Later, when preparing vaccines from the tissues of infected dogs, it was found that in the majority of cases the liver, spleen and mesenteric gland could all be used, since a mixture of these organs contained a sufficiently high concentration of virus to produce an efficient vaccine.

In all cases one part of the infected organs was emulsified with four parts of saline solution, and after the removal of a small sample so that the virus content could be estimated, sufficient formalin was added to bring the concentration of formaldehyde to 1 in 1,000. This rapidly (always in twenty-four hours) inactivated the virus, but the vaccine was kept for four days in cold store 0° C. to + 5° C. before being tested for sterility, and at this period sufficient strong ammonia was added to bring the pH to 8·2, a procedure which destroyed any formaldehyde remaining in the mixture.

In the case of vaccines prepared from infected ferrets, the spleen was taken about the fourth day of the disease, shortly before the animal would have died. Vaccines made from the infected liver, spleen and mesenteric glands of dogs were prepared from these organs taken at the height of the secondary fever when the animals were very ill; the period after infection was from seven to sixteen days.

The procedure recommended by the authors for the production of a really solid immunity was to give a dose of vaccine, and at the end of a week or ten days, a dose of living virus. This latter should be followed by no recognizable—or only very slight—symptoms of illness.

Some other very interesting points were elucidated in this work. It was found that a single dose of a vaccine made from the tissues of ferrets would produce satisfactory immunity in the ferret, but that in the case of the dog three doses given at weekly intervals were necessary before a degree of immunity was produced rendering it safe to give a dose of living virus. When vaccines prepared from the tissues of the infected dog were employed, a single dose was found to protect dogs satisfactorily against the injection of active virus, but no recognizable immunity was produced in ferrets, even after three large doses had been given at weekly intervals.

Borna's Disease.—Recently Nicolau, Galloway and Stroian (1929) have successfully immunized a limited number of rabbits against the virus of Borna's disease. In

these experiments the central nervous system of a rabbit dead from this virus was emulsified in a carbol-glycerine solution, the technique employed being similar to that used by Umeno in the case of rabies, and Todd in fowl plague. This vaccine became non-infective after six days at 26° C., and when injected subcutaneously in a single dose of 1 c.c., after keeping it at 26° C. for seven, eight or nine days, the animal was found to be immune when tested by intracerebral inoculation about seventy days later.

Previous experiments carried out with a vaccine prepared from the central nervous system of an infected rabbit inactivated with formaldehyde instead of the carbol-glycerine mixture, gave very inconstant and unsatisfactory results, although large repeated doses were employed. Formaldehyde, however, in strength employed —0·2 per cent. of formalin rapidly inactivated the virus.

Yellow Fever.—Hindle (1928 and 1929) has claimed that monkeys (*Macacus rhesus*) can be constantly immunized against yellow fever by vaccine made from the liver of a monkey dead from yellow fever, by the same method as that employed by Todd for his fowl plague vaccine, or by the use of formaldehyde. Aragão (1928) also stated that a vaccine prepared from infected monkey's tissue inactivated with 0·5 per cent. phenol, together with 0·2 per cent. formaldehyde, provided a satisfactory vaccine for these animals. These results, however, are difficult to confirm as it has been found that the virus of yellow fever may fail to infect some monkeys, especially when it has been passed through a large series of these animals. The successful results of vaccination claimed to have been carried out on man with vaccine made from monkey's tissue are all open to criticism.

Rinderpest.—Daubney (1928) employs a vaccine made from infected spleen inactivated with formalin. Jacotot (1929) recommends a vaccine made from various infected organs against rinderpest. Both authors claim excellent results. Jacotot also employs formalin as the inactivating agent; he also notes that vaccine prepared from the tissue of infected bovines forms an unsatisfactory vaccine for goats, and is even less efficient for pigs.

Let us now review these results. First of all, let us consider the inactivating agent. With some viruses—for instance, distemper—the infected tissue can be inactivated with heat, formaldehyde or phenol, and as long as the original material is rich in virus a satisfactory immunizing agent results. Heat is the least satisfactory agent. The above is probably true of the virus of foot-and-mouth disease, except that heated virus has never given satisfactory results.

Turning to fowl plague, Todd found that formalinized virus never produced more than partial immunity, while repeated doses of a vaccine inactivated with a carbol-glycerine solution constantly gave absolute immunity against many thousand infective doses of active virus.

Formalinized vaccines also were found to be unsatisfactory in the case of Borna's disease (Nicolau, Galloway and Stroian), and this is usually considered to be the case as regards rabies, but in both these diseases a vaccine prepared with a carbol-glycerine solution produces good immunity. The virus of vaccinia inactivated completely so that no pock is produced whether by heat, formaldehyde, phenol, or any other method, is apparently incapable of producing any useful degree of immunity.

Lastly, as regards the tissue from which the vaccine is prepared, Todd has shown that, although in the case of fowl plague liver emulsion can be inactivated constantly by the carbol-glycerine solution, which he recommends, in a maximum of five days, washed blood-corpuscles rich in virus treated with the same proportion of the antiseptic, remain infective for at least fifty-three days.

Considering the source of the virus—by this I mean the species of animal from which the tissues are obtained—Laidlaw and Dunkin, in the case of distemper,

show definitely that vaccine made from an infected ferret is effective in producing immunity in the ferret when a single small dose is given; in dogs, however, three doses are required to produce satisfactory immunity. Conversely, vaccine made from dog tissues immunizes dogs when a single dose is administered, but large repeated doses fail to produce a satisfactory immunity in the ferret. Jacotot also noticed that in the case of rinderpest, vaccine prepared from bovines was unsatisfactory when used to immunize goats and still less satisfactory in the case of pigs, although it produced a high degree of immunity in cattle.

However, we note that Vallée and his co-workers found, in the case of foot-and-mouth disease, that a vaccine prepared from the tissues of guinea-pigs produced solid immunity when injected into cattle, and was apparently as efficacious as a vaccine made from virus obtained from the bovine species.

It will thus be seen that no general rule can be laid down for the production of an inactivated virus vaccine. Each virus must, at present, be attacked as a separate problem, and only after experimenting with all the known methods will it be possible to say which is the best method. In the future, new and better methods may be devised, and perhaps these may have a more general application, but at present there is no guarantee that any two viruses will behave in a similar manner. Even the assumption that, because a vaccine prepared from the tissues of infected monkeys will efficiently immunize and protect uninfected monkeys, it will therefore protect man, is a very dangerous supposition.

You will have noticed that I have said nothing on the vexed question of whether these inactivated vaccines are living or dead; the reason is that there is no conclusive evidence in either direction. Most of the evidence which is available points in the direction of the latter assumption, and I believe that the more general opinion is that inactivated vaccines contain only dead virus, but there are some who believe that these inactivated virus vaccines contain virus which, although incapable of producing symptoms of the disease, can still propagate in the tissues for a certain time and thus bring about immunity against a natural or artificial infection. At present we must bring in a verdict of "not proven" to either view.

I now pass on to some of the problems concerning the mechanism of the immunity produced either by the recovery from an attack of a virus disease, or by a successful vaccination with an attenuated or inactivated virus.

It has long been known that in certain virus diseases, after recovery from an attack or successful vaccination with a modified or inactivated virus, the blood-serum contains protective antibodies; as instances I may cite rinderpest, vaccinia and rabies.

These protective antibodies were usually considered to be viricidal and to act on the virus much in the same way as protective or curative sera do against bacteria or their products. It must be remembered that even in the case of bacterial disease the action of antibacterial sera, using this term in a broad sense, is still only partially understood. However, from the mass of experimental data available, we do know when such antisera are treated with the corresponding antigen *in vitro* a binding takes place between the antibody and the antigen so that the antibody is absorbed from the serum. Further, the amount of antibody absorbed is, in general terms, proportional to the amount of antigen present, and in the final stage this union becomes a very firm one.

During the last two years a considerable amount of work has been carried out to ascertain if these general laws, almost universally accepted for antibacterial sera, apply to those protecting against viruses. Todd (1928), working with fowl plague, showed that a dose of virus mixed with just sufficient serum of an immunized fowl to render it non-effective on intramuscular injection, became infective when diluted or even without dilution when it was injected intravenously. This took place even

when the virus-serum mixture had been in contact for twenty-four hours. Andrewes (1928) found this also to be the case with vaccinia and its antiserum. Andrewes also found that when a virus-serum mixture containing a large excess of virus—above the quantity necessary to neutralize the action of the antibody in the serum—was kept at room temperature for various intervals up to twenty-four hours and then filtered, antibody could always be demonstrated in the filtrate. In these experiments which were, in the first place, carried out with vaccinia, the filter held back all the virus, but allowed the passage of the antibody, which was found to be present in practically the same concentration as in the original mixture.

Converse experiments were also made in which active virus was recovered from a virus-serum mixture containing a large excess of antiserum, after the mixture had been kept at room temperature for various intervals up to twenty-four hours. The usual technique employed was to cause a precipitate of euglobulin to form in the serum-virus mixture by dilution followed by saturation with carbon dioxide. During the precipitation the virus only was adsorbed on to the euglobulin, which was then collected, washed and redissolved. The resulting solution was then tested for the presence of virus by intradermal injection into rabbits. The virus can also be recovered by adsorption on to kaolin.

Other results obtained by Andrewes working with vaccinia, which bear on this problem are :—

(1) When mixtures of serum and virus are injected immediately after their preparation, the serum is as effective in modifying or preventing the formation of a local lesion as those that had remained at room temperature for twenty-four hours before injection.

(2) When both virus and serum were given intradermally no local reaction was observed when the serum and virus had been mixed previous to the injection, or when the serum was injected before the virus. When, on the contrary, the virus was injected even five minutes before the serum, a definite lesion was always produced.

(3) When attempts were made to titrate out the strength of an antiserum by intradermal injection in rabbits, very discordant results were obtained. Thus, with the same series of serum-virus mixtures the results shown in one animal indicated that the antiserum possessed a very considerable protective action, while in another animal only a very slight protective action could be detected. It may be mentioned that these divergencies were, according to the author, much greater than those seen when simple virus is titrated out on different rabbits.

Mixtures of serum and virus which gave no reaction when injected into the skin would give a very definite reaction when injected into the testicle.

Similar experiments carried out with Virus III gave comparable results, except that neutral serum-virus mixtures could not be re-activated by dilution.

From these experiments it appears probable that as regards vaccinia and Virus III, and, perhaps, some other viruses, antiserum-virus mixtures behave very differently from an antibacterial serum mixed with the corresponding bacterium or its products. However, this is by no means the universal view. Bedson (1928), working with herpes virus adapted to cause skin lesions in guinea-pigs, found that serum-virus mixtures injected shortly after their preparation produced lesions, whereas another portion of the same mixture kept for four hours failed to produce any lesions. From these and other experiments he came to the conclusion that the virus of herpes does unite *in vitro* with the antiserum, and states that at the time of writing there was no reason to believe that antiviral sera act differently from antibacterial sera. I believe this view is held by many other pathologists. Obviously, further investigations are necessary before a definite view, acceptable to the majority of experimenters, can be attained. During the current year Andrewes (1929), in this country, and Rivers (1929), in America, have attacked this problem from another point of view. Andrewes found that Virus III would propagate freely in a modified type of tissue cultures. These consisted of fragments of rabbit testicle

bathed in dilute plasma or serum. This in reality is not true tissue culture, but rather tissue survival with some migration of cells from the fragments of tissue.

Not only did Andrewes find that the virus propagated freely in such cultures and subcultures, but also that, if propagation of the virus took place, sections made from the fragments of testicle after incubation for from three to five days with the serum and virus mixture bathing it, showed numerous nuclear inclusion bodies in certain of the surviving cells. So constant was this finding that it was assumed that if inclusion bodies were found in sections of the fragments of testicle, propagation of the virus had occurred in the culture.

Working with this technique the following results bearing on the question of immunity have been attained :—

(1) When normal testicle and normal serum were employed as the culture medium together with a small trace of virus, propagation of the virus always took place and inclusion bodies were always found in sections of the fragments of testicle after from three to five days' incubation at 37° C. Subcultures showed the same phenomena up to many generations and these subcultures were always infective when inoculated into animals.

(2) When virus was added to cultures containing immune testis together with immune serum, no inclusion bodies were formed, neither did the virus propagate, or even survive for three days as shown by animal inoculation.

(3) When normal testis and immune serum formed the culture medium, no propagation of the virus could be detected either by search for inclusion bodies or by animal inoculation. This was only true when the virus was mixed with the immune serum before being added to the emulsion of testis, or when the immune serum was added before the virus. If, however, the virus was added to such a culture medium even ten minutes before the immune serum, and the culture was kept at a temperature of 37° C. during the interval between the addition of virus and immune serum, inclusion bodies were always found in the sections of the testicular fragments.

(4) When immune testis and normal serum were used as the culture medium, inclusion bodies were found in section of the tissue and the cultures were infective when inoculated into animals. When the immune tissue was washed in Tyrode's solution so as to remove any traces of immune serum, this was constantly the case. These results are surprising, considering the claims made by several authors of a high degree of cellular immunity. Experiments similar to these have been made independently by Rivers in America, employing vaccinia virus, and his conclusions have been in almost complete agreement with those of Andrewes.

The use of modified tissue cultures opens up a new method for investigating the mechanism of immunity and other problems in virus diseases. Another advantage is that it provides a method which will greatly lessen the number of animal inoculation tests necessary in carrying out work on virus diseases. It must be remembered, however, that the final proof of any conclusion arrived at by such means must be confirmed whenever possible by tests on the living animal.

Taking even the researches mentioned—and there are many others of equal or greater merit, which, if time allowed, I might have included—I think you will acknowledge that considerable progress has been made in the study of virus diseases during the last two or three years, but how much remains to be done! As regards human virus diseases, the difficulties are even greater than in the case of animal diseases, since, at present, many cannot be transmitted to other animals, and even when this transmission is possible the infection cannot be carried on always through a series of animals, for instance; this is the case with experimental measles in monkeys. At present, therefore, we must be content to continue to study those diseases which can be transmitted to animals which can be easily kept and bred in large numbers. Instances of the importance of this is seen in the researches on distemper, when ferrets could be used in large numbers instead of dogs; and in the use of the guinea.pig in the case of foot-and-mouth disease. It must be remembered always, however, that the final proof must be carried out on the animal in whose interest the investigation was undertaken.

For the time being we must study each separate virus disease as a separate entity, so that in time to come we may be able to formulate some more or less general laws in connection with these diseases.

Lastly, let human and veterinary investigators work hand-in-hand to gather new facts and devise new methods, and when any results are obtained having a practical application let human or veterinary practitioners test such procedures in the field or the hospital with due care and just criticism, so that their true practical value may be quickly ascertained.

BIBLIOGRAPHY.

VALLÉE, H., CARRÉ, H., and RINJARD, P., *Rev. gén. de méd. vét.*, 1926, xxxv, 129; *ibid.*, 1928, xxxvii, 257. TODD, C., *Brit. Journ. Exper. Path.*, 1928, ix, 101; *ibid.*, 244. UMENO, S., and DOI, Y., *Kitasato Arch. Exper. Med.*, 1920-21, iv, 89. LAIDLAW, P. P., and DUNKIN, G. W., *Journ. Comp. Path. and Therap.*, 1928, xli, 1; *ibid.*, 209. JACOTOT, H., *Arch. Inst. Pasteur Indochine*, 1929, No. 93. NICOLAU, S., GALLOWAY, I. A., and STROIAN, N., *Compt. rend. Soc. de Biol.*, 1929, c, 607. HINDLE, E., *Brit. Med. Journ.*, 1928 (i), 976. *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1929, xxii, 405. ARAGÃO, *Mem. Inst. Oswaldo Cruz*, Suppl., No. 2, 23. BEDSON, S. P., *Brit. Journ. Exper. Path.*, 1928, ix, 235. DAUBNEY, R., *Journ. Comp. Path. and Therap.*, 1928, xli, 228; 263. ANDREWES, C. H., *Journ. Path. and Bact.*, 1928, xxxi, 671; *ibid.*, 1929, xxxii, 265. *Brit. Journ. Exper. Path.*, 1929, x, 188; *ibid.*, 273. RIVERS, T. M., HAAGEN, E., and MUCKENFUSS, R. S., *Journ. Exper. Med.*, 1929, l, 665.

Section of Ophthalmology.

[*January* 10, 1930.]

Melanotic Sarcoma of the Choroid.—A. F. MacCallan, C.B.E., F.R.C.S.

Patient came under observation only three days after noticing that sight of right eye had become defective.

Vision: (R) hand movements; (L) $\frac{6}{5}$.

A tumour in the inner part of the fundus, seen with the naked eye by focal illumination, occupies the ciliary region and stretches back to the optic disc. It is best seen with a + 8 sph. in the ophthalmoscope. One or two vessels running over it show that the retina is detached.

The diagnosis seems to lie between an inflammatory detachment—by some called a serous detachment—a cysticercus (the patient having resided in countries where this is prevalent and having had malaria and dysentery), and a sarcoma of the choroid.

There was no eosinophilia, and a complete examination of the stools excluded the presence of any parasite.

Radiography of the orbit showed normality, but a root abscess in the right upper jaw was detected. Further dental radiography showed the presence of two apical abscesses. Expert dental opinion then being obtained, it was decided, on purely dental grounds, to remove the remaining teeth. At this point there seemed to be grounds for believing that the tumour was inflammatory in origin, that is to say, was an ordinary detachment of the retina, resulting from a septic focus in the teeth.

The tonometric reading with Maclean's instrument was 16 in the affected eye and 22 in the good eye.

There was a small retinal hæmorrhage to the outer side of the right optic disc, and eleven days after the patient came under observation, I thought that the tumour seemed a little fuller.

The eye was therefore removed and found to contain a melanotic sarcoma, which did not penetrate the sclerotic.

Microscopic Sections.—These show a circumscribed sarcoma, slightly pigmented in parts and probably arising from the outer layers of the choroid. The cells are spindle-shaped, but some are cylindrical—these are spindles cut at a different angle. The tumour is fairly vascular.

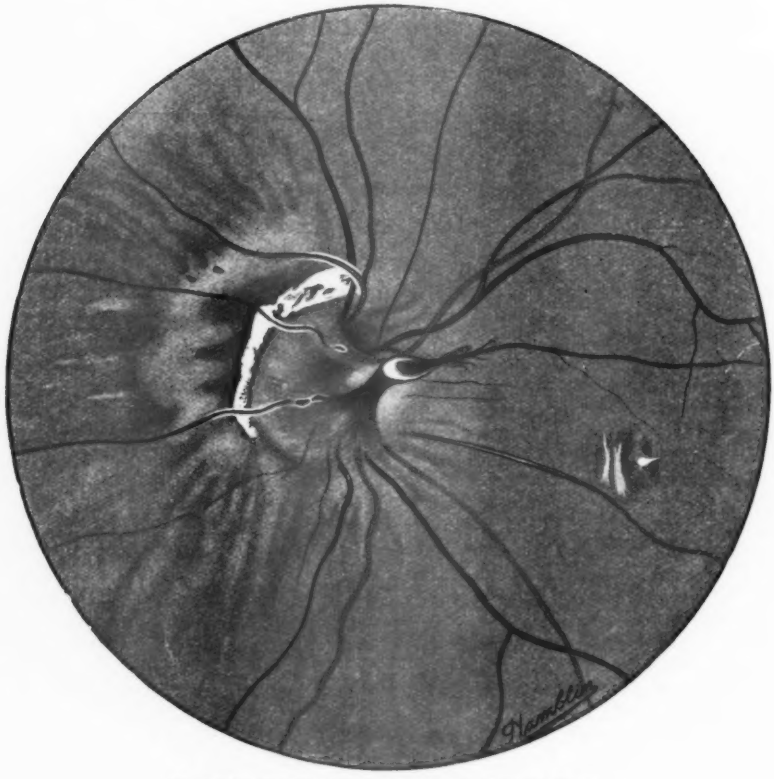
There is no evidence of extra-ocular extension through the usual channels. The angle of the anterior chamber is free. There is a detachment of the retina.

Persistent Hyaloid Canal (Canal of Cloquet) in Left Eye.—L. M. Smith Clark, M.B.

K. S., a boy, aged 10. Attended School Clinic, December, 1929, and was referred by Dr. Marjorie Dalby for defective vision in left eye.

Vision: Right, $\frac{6}{6}$ normal; left, $\frac{6}{18}$; not improved with any lens. The canal of Cloquet is persistent in the left eye, extending from the optic disc and coming right

forward to the posterior capsule of the lens. It tapers in its central part, and in this narrowed extent there appear to be the remains of the hyaloid artery. There is a rupture of the choroid at the inner side of the optic disc.



Dr. Smith Clark's Case of Persistent Hyaloid Canal.

Discussion.—Mr. J. GRAY CLEGG said that near the disc there was an appearance as if a rupture of the choroid had occurred. He wondered how that could be accounted for. He asked whether instruments were used at the birth of the boy, and whether there was hæmorrhage into the canal of Cloquet.

Dr. SMITH CLARK (in reply) said that no instruments had been used. The birth had been premature (about the end of the eighth month) and precipitate. It was difficult to account for the rupture of the choroid unless it was caused by an accident at birth. She thought the appearance of hæmorrhage was really due to partial persistence of the hyaloid artery.

Epibulbar Papilloma.—ARTHUR GRIFFITH, F.R.C.S. (shown by Mr. A. F. MACCALLAN, F.R.C.S.).

H. D., male, aged 63.

History.—Red swelling on right eye, first noticed in August, 1929. Increasing in size. This tumour is roughly rectangular in shape and measures 1 cm. in its

greatest horizontal and vertical directions. Its elevation from the surface of the conjunctiva is $1\frac{1}{2}$ mm. It moves easily with the conjunctiva over the sclera, but is firmly attached to the temporal side of the cornea for 1 mm. It is rose-pink in colour. Its surface is dull, and looks shaggy. It is this appearance especially which suggests the diagnosis of papilloma of the conjunctiva. I propose dissecting the tumour away from the eye, and carrying out a plastic operation on the conjunctiva.

Mr. A. F. MacCallan asked whether, in the opinion of Members, the growth was innocent or malignant; also whether local removal should be attempted, and if it were found to be malignant whether it should be treated with radium.

Mr. Humphrey Neame, in reply to Mr. MacCallan, said that if the growth was angioma it was entirely simple; if endothelioma, it would possibly become malignant. It was encroaching on the edge of the cornea, and this made him more inclined to think it was endothelioma, and therefore malignant. He would shave it off freely, taking away some of the corneal substance. He would base the subsequent action on the microscopic diagnosis, deciding as to radium treatment afterwards.

Demonstration of the Theory of Vision.

By F. W. Edridge-Green, C.B.E., M.D., F.R.C.S.

All the facts of vision show that the cones of the retina are the percipient elements and that the rods of the retina are the nervous elements which sensitize, by means of the visual purple, the liquid surrounding the cones and that they themselves are not percipient elements. The central portion of the retina, the fovea, corresponding to the area of most acute vision, contains only cones and therefore is sensitized from the periphery, there being a steady flow of sensitized liquid into this area.

The following simple experiment demonstrates this flow. Colours which only stimulate the para-foveal regions are carried into the central region until this region is covered by them.

Place a piece of black cardboard, eight inches square, on a wallpaper with a coloured pattern. The light in the room should not be too bright, but the experiment can be done easily in an ordinary room with the daylight of the present time. The black cardboard should be viewed with one eye at a distance of 6 ft., the eye being kept as immovable as possible. It will then be noticed that portions of the colours of the wallpaper will appear to detach themselves from the paper and move with a slow spiral motion into the black area. This will go on until the whole black area has completely disappeared, the surface being covered with a mixture of colours similar to those on the wallpaper.

If a Persian carpet be used for the purpose of the experiment, the area will be covered with a mixture of the colours of the carpet. If a uniform colour be used the black area will be covered by that colour. It may even make another colour disappear. For example, if a piece of red paper an inch and a half square be placed on a piece of yellow-green cardboard the yellow-green will invade the red until only a yellow-green surface is seen. If any difficulty is experienced, the experiment should be tried in a dimmer light, but I have not found anyone, as yet, who has not seen the phenomenon with ease.

Discussion.—Mr. R. Lindsay Rea said he watched this with his right eye while his left was covered and he noted the middle of the black object become pink. He then quickly covered the right eye and looked with the left, and at once saw the same with that eye, though it had not been staring at it. He therefore thought the phenomenon was really a mental impression.

When he first looked, he saw pink in the middle, and then pink in the eye which he first covered. Why did blinking restore the view? [The PRESIDENT said he noticed the same thing himself.] He admitted that, on looking at the second illustration, he saw the surrounding colour invade the edges of the dark object.

Mr. RANSOM PICKARD said that when he looked at the black card, not knowing what he would see, he saw first a green pattern, like that of the surrounding carpet, and he failed to see how a pattern could be evident except as a cerebral event.

Mr. DAVID WILSON said he did not quite follow Mr. Edridge-Green's reasoning. In the experiment shown, what happened in his case was that the black object on the red ground began to disappear from sight, and then the whole thing went completely black. He would like an explanation of that.

Dr. F. W. EDRIDGE-GREEN (in reply): Mr. Rea probably saw an after-image, and it was not being seen by the left eye at all. In answer to Mr. Pickard, the movement was obviously in the retina. I evolved this experiment by deduction. The colours moved in a spiral way, and in the centre the observer would soon see whirlpool movements.[1] If one looks at a patterned Persian carpet, one sees a pattern which blends with the carpet, but it is not the actual pattern which is seen. The colours of the pattern are there, but they are mixed up. The correct appearance in this experiment ought to be seen in from five to ten seconds, then darkening begins.

I have discussed this theory with von Kries, who said that my theory of vision explained numerous facts for which his failed to account, and at an International Physiological Congress at Gröningen, Professor Arrhenius said he was firmly convinced that I had set forth the correct theory of vision.

When I propounded this theory at the International Medical Congress at Budapest my paper was read by special request in two sections. Not only was there no dissent but there was most emphatic approval. Professor A. von Tschermak, of Vienna, one of the world's leading authorities on vision, said that there was not a single fact or deduction in my paper that he could not support from his own observations and he subsequently wrote to the *Lancet*[2] supporting my views.

Ferree had shown that in the case of different after-images a red after-image might go right through a green one on moving the eye; and stated that the only way to move these colours was to move the eye. There are two ways in which one can get movement of the visual purple. One is the steady movement which is always going on, except, perhaps, during sleep, and the other by moving the eye. Helmholtz timed the circles. When the eye was moved, the eye-muscles put pressure on the retina and drove the fluid in an irregular way. My explanation of miners' nystagmus is that when confronted with the black surface of the coal face, the visual purple does not flow in to the fovea properly in the absence of peripheral stimulation, and to get it to flow in the miner moves his eyes.

Krukenberg's Spindles.—J. D. MAGOR CARDELL, F.R.C.S.

Patient, male, aged 42, seen at Central London Ophthalmic Hospital, May 13, 1929, complaining of diminution of vision, following a blow on the left eye. On examination it was found that both eyes were myopic:—

$$\left(\text{Right with } \frac{-2{\cdot}25}{-1{\cdot}0} = \frac{6}{6}, \text{ and left with } \frac{-2{\cdot}75}{-1{\cdot}5} = \frac{6}{9}\right).$$

It was further noted that there was an opacity on the back of both corneæ. When viewed with the loupe the opacities were seen to be roughly oval in shape, about 4 by 2·5 mm. in size, russet brown in colour, with the long axis of the oval placed obliquely, and the centre of the oval about 2 mm. below the centre of the cornea. The colour of these opacities was the same as that of the irides. No persistent pupillary membrane; no sign of iritis; fundi normal.

The patient was then examined by the slit lamp, when it was found that, though the main and more definite opacity occupied the central part of each cornea, the whole of the backs of the corneæ, with the exception of the temporal quarter of the

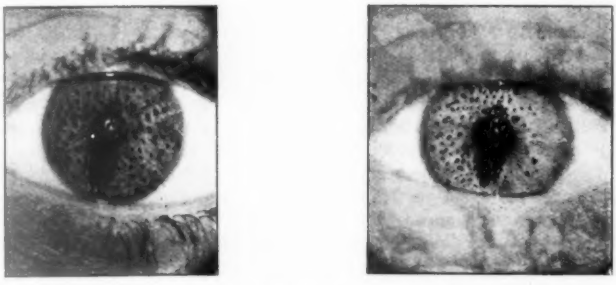
[1] See "The Physiology of Vision," 1920, 90.

[2] 1909 (ii), 1308.

left cornea, were peppered with very fine particles of pigment, which, by being more thickly deposited centrally, gave rise to the first impression that the opacities were defined ovals. Furthermore, pigment was found circulating in the anterior chamber of the left eye, but not in that of the right. The iris of both eyes was sprinkled with pigment, but none was seen in the retrolental space (fig. 1).

The only change that had occurred at the end of five weeks was that the circulation of pigment had ceased in the left eye. Since that date the patient had been lost sight of.

This case varies in some particulars from that which I showed here in 1925,[1] the patient being a woman aged 30. The particles of pigment lay just anterior to



R FIG. 1—1929. L

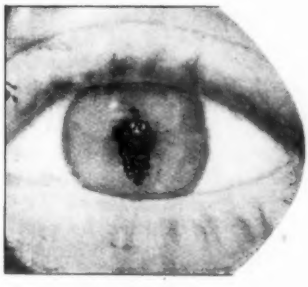


FIG. 2.

Descemet's membrane and were in the shape of minute rings with clear centres (fig. 2).

Miss Mann examined that case with me and localized the position of the pigment. It is the only case of those examined by the slit lamp in which the pigment did not lie on the back of Descemet's membrane.

Though forty-one cases have been observed, I have only been able to trace details of thirty-one since 1899. Summaries of cases are given by Holloway (*Annals of Ophthalmology*, 1910, xix, 685), and Koby (*Revue Générale d'Ophtalmologie*, 1927, xli, 53).

From the brief historical synopsis of these thirty-one cases given at the end of this paper, I give here the following salient facts.

[1] *Proceedings*, 1925, xix (Sect. Ophthal.), 1.

(1) 71·4% were females. (2) Average age 46·2. (3) Bilateral in 93·8%. (4) Myopia in 80%. (5) In 26·7% there were congenital defects. (6) In 20% associated inflammation.

The question as to whether the condition is congenital or acquired has not yet been decided, though the greater weight of opinion seems to be on the latter side. The arguments advanced in favour of the congenital theory are:—

(1) Symmetry. (2) Females predominate. (3) Pigment spots of the same size. (4) The eyes are, with one or two exceptions, myopic. (5) Has been observed in mother and daughter in three instances. (6) No past history or indication of inflammation. (7) Pigment is interstitial in position.

Against these arguments it may be said: (1) There is not always symmetry. (2) Certain types of disease show a predominance in one sex. (3) A myopic eye tends to be unhealthy and more liable to inflammation. (4) Koby has observed the spindles forming in two cases, one of which has antecedent iridocyclitis. (5) Of those cases that have been examined by the slit lamp, only in that described by myself in 1926 was the pigment interstitial. (6) I have myself, in the last four years, examined about 4,000 school-children, aged 5 to 14, and have never seen a Krukenberg's spindle, nor do I know of any recorded case at this age.

An interesting fact in the second case I have seen is that the back of the *right* cornea was peppered all over with pigment, and no pigment was seen circulating in the anterior chamber, while in the *left* eye, though pigment was circulating in the anterior chamber, ready to be deposited, the temporal quarter of the cornea had no pigment upon it. The circulation of pigment in this eye might easily be explained by the blow, but it is evident that some other factor must be present to determine the adherence of pigment to the back of the cornea.

Koby says that two factors are necessary for the production of a spindle:—(1) Circulation of the aqueous. (2) Disintegration of pigment associated with myopic uveitis, glaucoma, etc., the pigment being of retinal rather than meso-dermal origin. He thinks that the endothelial cells are injured by the rubbing of the pigmented particles against them, with the result that they take up the pigment which becomes located in the interior of the cells. He explains the interstitial position of the pigment in some cases by saying that the endothelial cells once having taken up pigment, may pass it forward into the layers anterior to them.

Now circulation of pigment in the anterior chamber is often seen after blows upon the eye and intra-ocular operations. In one case of cataract extraction I have in mind, at the end of four days pigment settled on the back of the cornea in such a manner as to cause the nurse who dressed the eye to report a hyphæma. Its lodgment on the back of the cornea was so evanescent that when the house-surgeon saw the case the "hyphæma" had disappeared. The phenomenon was explained on examination with the slit lamp. In this case the pigment did not pass out of circulation until about a week later, showing that the "scrubbing" of the endothelium by the pigment suggested by Koby, does not occur in all cases, and that, even given pigment resting upon the endothelium after having been in circulation, there must be postulated some factor which causes the cells to take up the pigment. In another of my cases—that of a young man—after a blow upon the eye, pigment came to rest temporarily upon the back of the cornea. In neither of these two cases did any figure resembling a Krukenberg's spindle ever show itself while they were under my observation.

With regard to pigment passing forward into the more anterior layers of the cornea, I have examined, with the slit lamp, pigment on the back of the cornea which has been present for years, but have not yet observed any case in which it has altered its position.

Again, if the cause is inflammatory, there should have been a sufficient number and diversity of inflammations of the eye in such a long period as thirty years, to have produced more than forty-one recorded cases of Krukenberg's spindles.

The first case I saw was, I think, of a congenital nature, but I must confess that the second case leaves me in some doubt. On the whole, however, the theory of a congenital origin is, to my mind, slightly the more acceptable.

Review of 31 Cases of Krukenberg's Spindles.

The details obtainable are not complete in every case. Of the 31 cases, 20 were in females and 9 in males, the youngest being 17 and the oldest 68. The condition was bilateral in 15, unilateral in 1, the spindle being of the same colour as the iris in 8, of different colour in 4, and the average size 4 × 2 mm. The spindle had its major axis vertically in 5, obliquely in 3. In 4 the pigment extended beyond the central figure.

Associated ophthalmic defects in the anterior chamber and iris were congenital in 4, acquired in 3, no defects in 8. Inflammatory changes of the deeper parts of the eye were seen in 7, lens opacities in 6, myopia in 20, emmetropia in 3, and hypermetropia in 2.

The average picture presented is therefore a vertical spindle, 4 × 2 mm., of the same colour as the iris, present in both eyes of a myopic female aged 46.

Chronological List of Observers and Number of Cases described by each.

1899, Krukenberg 3. 1900, Weinkauff 1. 1901, Stock 2. 1903, Thompson and Ballantyne 1. 1911, Hess 1. 1912, Augstein 6. 1913, Streber and Steiger 6. 1917, Kraupa 5. 1920-21, Vogt 4. 1923, Haussen 1. 1925, Koby 2. 1925, Cardell 1. 1926, Sallman 1. 1926, Seissinger 3. 1927, James 1. 1929, Friedman 1. 1929, Cardell 1.

REFERENCES.

CARDELL, *Brit. Journ. Ophth.*, 1926, x, 198. JAMES, *Brit. Journ. Ophth.*, 1927, xi, 148. FRIEDMAN, *Arch. Ophth.*, 1929, i.

A Microphthalmic Family.—EUGENE WOLFF, F.R.C.S.

So few microphthalmic families resembling this have been recorded that I thought it was worth bringing to the notice of this Section.

The parents were first cousins, their mothers having been sisters. There are ten children alive of whom five, three males and two females, have small eyes. The affected ones were the first (Elizabeth), the third (Rose), the fourth (Ivy), the eighth (George), and the tenth (Edward), who is really the eleventh, as the eighth child had a twin brother who died.

In the majority of recorded cases of microphthalmos there has been some other congenital malformation such as cataract, or coloboma of the iris and choroid often combined with nystagmus. In the majority, too, there has been poor vision even with correction. The affected members of this family, however, simply have small eyes without any of the above defects. They are all high hypermetropes with relatively little or no astigmatism, and they all had reasonably good vision, at one time, at any rate. A variable amount of pseudo-neuritis is present. There is also some ptosis associated with narrow palpebral fissures (2·1 cm. in width) and small orbits (vertical height 2·5 cm.). The eyes are deeply set so that—as I think Scherenberg was the first to point out—the lower orbital margin, which normally makes no prominence, is visible.

It is difficult to decide when to call an eye microphthalmic, since all grades, from anophthalmos to the normal eye, are found. It is not possible to measure the antero-posterior diameter of the eyeball, and the size of the cornea is not an absolute

indication. In my cases the cornea measured about 10 mm. in transverse diameter. Yet these eyes are obviously not small, only in the sense of the amount visible, that is in the size of the palpebral fissure.

The following is a record, which I have verified, of the refractions and visions in four of them. The fifth child with small eyes wears glasses, but is in Canada, and I do not know the amount of error.

Elizabeth (1), right vision with D. sph. + 15 = $\frac{6}{18}$; left vision with D. sph. + 15 = $\frac{6}{18}$. Remains of hyaloid artery in the left eye near the disc.

George (8), right vision and left vision with $\frac{\text{D. sph. } + \ 14{\cdot}5}{\text{D. cyl. } + \ 1{\cdot}5} = \frac{6}{9}$

Edward (10), right vision with D. sph. + 15 = $\frac{6}{12}$; left vision with D. sph. + 15·5 = $\frac{6}{9}$.

Ivy, the fourth child, has been the most unfortunate. At 5 years of age she had the left canaliculus slit for epiphora. In 1923 she suddenly lost the vision of the right eye. When seen in February, 1924, she had no P.L. in this eye and had a cupped disc. Later a secondary cataract developed.

$$\text{Left vision with } \frac{\text{D. sph } + 13}{\text{D. cyl. } + 1{\cdot}5} = \frac{6}{12}$$

In February, 1928, she had an attack of subacute glaucoma in the good eye. This was trephined in March, 1928. Then a cataract developed and was extracted. It was difficult even on drawing the eye forwards to make the section, owing to the globe being so deeply seated in the orbit. The section was corneal in an attempt to miss the trephine hole. There was surprisingly little reaction. She has since been needled twice, and now with a + 22 lens gets $\frac{6}{36}$.

As Priestley Smith points out, these cases are more liable to glaucoma because as a rule the eyes are not small in proportion, the lens being relatively too large. In eyes which are smaller still the lens is usually cataractous and small, and thus probably tends to save the eye from glaucoma. Priestley Smith has described the case of a man with abnormally small eyeballs, with clear lenses, who suffered from primary glaucoma and whose daughter, years later, presented just the same mal-development of the eye with increased tension.

The record of the highest hypermetropia that I could find was that of Roll, who described the case of a boy, aged 17, having a small cranium and a narrow and prominent upper jaw. Under homatropin and cocaine the hypermetropia was estimated at 20D. The vision was not improved beyond $\frac{6}{60}$.

The eyes just described are not nanophthalmic, a very rare condition, in which, although the eyes are small, their refraction is emmetropic (Parsons) and they are not infantile. Although Iwanoff (1898) found that in the newborn 92% were hypermetropic, the hypermetropia was never that seen in these cases.

Treacher Collins (1899) has pointed out that the diameter of the cornea in intra-uterine life is more than half that of the whole eye, while in the adult it is less.

With regard to the children affected, Laqueur says that the second child is less frequently diseased than the first and third and that the fourth is most often affected. In my cases it is interesting to note that the fourth child, a premature baby, was the most seriously affected, that the second was exempt and that the first and third had small eyes.

Reber, however, describes a family of five, in whom the first, second and fourth child were affected and the third and fifth exempt. They had micropthalmos, hypermetropia of 14D, and a grey disc, the size of the papilla, at each macula.

With regard to inheritance, Usher published a pedigree of microphthalmos with myopia and corectopia and gave a list of those cases that showed inheritance of microphthalmos. I could find no history of inheritance in my cases. The grandfather had cataract, but he was in the Navy before this, and his original reading glasses were D. sph. + 3. So he could not have had small eyes. Also George (No. 8) has two children and Rose (No. 3) has one child all with normal eyes. The unaffected brothers and sisters are also married and have normal children except Faith (No. 5) who had epileptic fits as a child.

None of my cases showed corectopia to any degree. The relationship between this condition and microphthalmos is fully described by Usher. One may, however, in passing mention that Best quotes an interesting observation of Kotelmann, who found that the position of the pupil tended to vary with the race, and that in Patagonians it was normal to have ectopia pupillæ upwards and inwards.

Dr. E. A. Cockayne kindly sent me the following quotation from Charles Darwin's "Animals and Plants under Domestication": "Mr. White Cowper says that in all cases of double microphthalmia brought under his notice he has at the same time met with defective development of the dental system."

As there is very little about this point in the literature, the following note may be of interest. Three of this family, Nos. 4, 10 and 7 had only two upper incisors. No. 7, it will be noted, is a male with good eyes. Ivy (No. 4) had four abnormally small lower incisors and George (No. 8) had supernumerary teeth. He is said to have had two rows.

In Brailey's case, that of a girl aged 18, the teeth were much more affected. Mr. Maggs reported on them as follows:—

Upper Jaw.—All the incisors are congenitally absent, also all the molars. Both canines are present, as also two premolars on each side. The total number (seven) is made up by one temporary molar remaining between the two premolars of the right side. *Lower Jaw.*—The incisors are wanting on the right side, the canine on the left. The second premolar and wisdom are wanting on each side. A supernumerary canine on the right side makes up the number—ten.

With regard to the causation of microphthalmos, there are two theories: (*a*) developmental and (*b*) inflammatory. Possibly in my cases the consanguinity of the parents may have been the exciting cause of an arrest of development. Syphilis has, however, been blamed in certain cases, although there was no evidence of it here. With regard to the second theory, the inflammation may be in the parent or the affected child. In this connection Deutschmann's experiment, quoted by Fuchs, is interesting. When tubercle bacilli were injected into a rabbit's eye, and the female rabbit lost its eye by infection, the young had microphthalmos and coloboma. The truth of this observation has, however, been disputed, and it is impossible here to go into this question more fully.

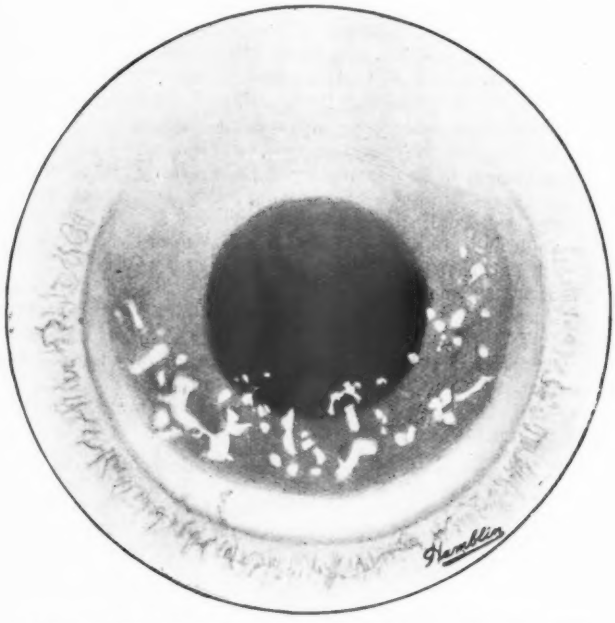
In conclusion I wish to thank Sir John Parsons and Mr. Humphrey Neame for kindly allowing me to publish the above observations on cases which came under their care.

BIBLIOGRAPHY.

REBER, M., "Mikrophtalmie compliquée d'hypermétropie excessive et d'anomalies de la macule, observé chez trois sœurs," *Ann. d'Oculistique*, 1898, cxix, 445. SCHERENBERG, K., "Beitrage zur Lehre vom reinen Mikrophthalmus." Inaug. Dissert. Tübingen 1900, ref. *Nagel's Jahresbericht*, 1900, 297. FUCHS, E., Discussion, Ophthal. Society on Bronner's paper on Microphthalmos, *Trans. Ophthal. Soc.*, 1902, xxii, 212. PARSONS, Sir J. H., "Pathology of the Eye." ROLL, G. W., "Microphthalmos," *Trans. Ophthal. Soc.*, 1903, xxiii, 398; and *Ophthalmic Review*, 1903, 177. BRAILEY, W. A., "Double microphthalmos with defective development of iris, teeth and anus. Glaucoma at an early age," *Trans. Ophthal. Soc.*, 1890, x, 139. BEST, F., "Korectopie," *Arch. f. Ophthal.*, 1894, xl, pt. iv, 198. DARWIN, CHARLES, "Animals and Plants under Domestication," 1893, ii, 321.

Calcareous Deposit on the Back of the Cornea.—ADRIAN CADDY, F.R.C.S.

The case was shown at the October meeting of the Section.[1] The illustration shows the unusual calcareous deposit on Descemet's membrane, which does not give the impression of being of the nature of calcification of keratic deposits.



Calcareous deposit on the back of the cornea (Mr. Adrian Caddy's case).

[1] *Proceedings*, 1929, xxiii, 45 (Sect. Ophth. 3).

Section of Neurology.

[*December* 12, 1929.]

Paralysis of the Oculomotor Nerve-trunks in Diabetes.

By James Collier, M.D., F.R.C.P.

For the past twenty-one years I have looked after a clinic of cases of medical interest at the Royal Eye Hospital, Southwark. Had my experience been limited to the National Hospital, Queen Square, it would have been a relatively narrow one. At the Eye Hospital one sees many rapid and transient ocular palsies and many cases in which ocular symptoms alone trouble the patient. Here years ago I became aware of cases, especially those occurring in later life, which did not correspond with the ætiology usually associated with ocular paralysis. Some of these—such as the transient sixth-nerve palsy which follows spinal anæsthesia—have since become well known; of these I saw several examples before any mention of the condition had been made in the literature. Again, there is the sixth-nerve palsy which seems to result from the same causes as Bell's palsy. I have seen this with Bell's palsy in a patient who made a complete recovery from both conditions. Ocular nerve trunk palsies are often multiple and associated with orbital pain and tenderness, and occasionally with involvement of the upper two branches of the fifth nerve, sometimes due to exposure to cold alone, but more often consequent upon the spread of inflammation from septic sinusitis, the "sphenoidal fissure syndrome." There is another group of which I have long been aware, though very little has been said of it in England, namely, that of paralysis of the oculomotor nerve trunks in diabetes, and it is with cases in this group that I propose to deal in this paper. A few months ago three new elderly patients with external rectus palsy presented themselves at the Royal Eye Hospital. In discussing the possible cause I suggested that we might find glycosuria in one of the three cases. On testing, we found that two of them gave copious sugar findings, and these two made complete and rapid recovery upon strict dieting. I must not convey the impression that diabetic ocular paralysis is as common as this experience would suggest, but it cannot be a very rare condition, for I have seen more than thirty cases in the past twenty years.

I shall give first, a short summary of my own cases, and then information I have gained from the literature. Finally, I will make a few remarks upon the possible morbid anatomy of the condition.

My patients, with the exception of two, were in good working health; they presented no other symptom of diabetes and no other sign of diabetic nervous involvement. In the majority the ocular paralysis was the earliest symptom, and its presence led to the discovery of the glycosuria. In one patient the glycosuria long preceded the palsy; in this case there was severe retrobulbar neuritis. Another who had been many times in hospital with cardiac and pulmonary disease, but without glycosuria, developed a terminal glycosuria with retrobulbar neuritis and total ocular paralysis. In all the cases, since the Wassermann reaction has been at our command, this test was made and was negative, with the exception of the last case. None of the patients presented any sign of tabes or of other nervous lesions. The youngest patient in the series was forty-two years old, and most of them were more than fifty years old; in this respect the condition is parallel with the vascular lesions of diabetes. The sex incidence was that of the causal condition.

The first cases that I saw made no improvement as regards the ocular paralysis, and knowing nothing about the meagre literature which then existed (the condition is not mentioned in that rich museum of clinical facts—Gower's "Manual of Nervous Diseases"), I thought that the oculomotor nerve-trunk palsies of diabetes were akin to the isolated nerve-trunk palsies of the limbs. These palsies of median, ulnar and

sciatic nerves, often multiple, are of rapid and painless onset. They are always total and never improve. I think they are due to thrombosis of the vessel supplying the nerve trunk, from a degeneration of the vessel wall similar to that in diabetic gangrene. I thought that the ocular palsies were due to such a thrombosis, and that they were permanent and admitted of no treatment. One day I wanted a case for demonstration at St. George's Hospital, and coming across one of right third and left sixth nerve paralysis with glycosuria, at the Royal Eye Hospital, I sent the patient into St. George's and dilated upon the thrombosis of the nerve-vessels and the hopeless outlook with regard to recovery. Afterwards my house physician demonstrated complete recovery of the nerves in the course of three weeks under a dietetic treatment alone. It is a remarkable fact that I have not since that time seen a single case which did not make complete recovery; this I think is in some measure due to careful dietetic treatment. The onset of the paralysis is usually rapid but not sudden; sometimes it occurs in a night. In one patient it occurred in hospital in the course of three days; first the third nerve, then the fourth, and then the sixth nerve on one side, followed by those of the other side in the same order. This patient was severely ill, and died soon after. The onset is painless, and is not associated with tenderness on pressure upon the eyeball or with proptosis, as are so many of the sphenoidal fissure lesions. I have never seen any implication of the first division of the fifth nerve.

Paralysis of the sixth nerve on one side is by far the commonest occurrence, and next, in order of frequency, paralysis of the third nerve on one side; then bilateral paralysis of these nerves in the same order; then combined paralysis of third and fourth nerves on one side, or of third and opposite sixth nerve, which I have seen in about the same number of cases. Isolated paralysis of the fourth nerve I have never seen, or rather I have never recognized it as glycosuric, though many observers have done so. Paralysis of one of the twigs of the third nerve has been rare in my cases; all I have seen has been paralysis of levator of eyelid and eyeball in one case, and internal rectus palsy in another. Isolated paralysis of the ciliary muscle, or of the light reflex, or of both, I have not recognized as others have. Total paralysis of all the oculomotor nerves on both sides has occurred once, in the case that proved fatal. Recurring paralysis, in spite of treatment, I have seen once. This was a most interesting case, brought to me by Mr. Williamson-Noble, that of a woman, aged 64, who had had glycosuria for years. In August, 1924, palsy of the right third and fourth nerves developed, and was complete, but the pupil was exempt. She had completely recovered from the paralysis by December of the same year. In June, 1925, acute retrobulbar neuritis of the left eye developed, with paralysis of the left third and fourth nerves, which was complete. There was recovery from the paralysis, but not from the severe amblyopia of the left eye. This patient has extensive fundal changes of the glycosuric type.

In all my cases the glycosuria has been high and diminution of the paralysis has been accompanied by a fall in the glycosuria and in the blood-sugar. That, however, has not been a universal experience, for sometimes the sugar content of the urine has been described as very low. It is interesting to note that E. W. Taylor refers to an association of sixth nerve paralysis with polyuria, though he does not refer to its association with glycosuria. K. Mendel in the *Neurol. Centrabl.*, 1918, 285, describes such a case and refers to five other cases in the literature, four of which were traumatic and therefore presumably associated with injury to the pituitary gland. Many cases of frank pituitary disease with the association of polyuria and sixth nerve palsy have been reported.

With regard to the literature of the subject: the first record that I can find of the association of diabetes and ocular paralysis came from St. George's Hospital, where sixty-three years ago Dr. William Ogle wrote a paper on the nervous

manifestations of diabetes, which was published in the St. George's Hospital reports for 1866. Of fifteen fatal cases he reports two in which, towards the end, bilateral third nerve paralysis and left facial paralysis occurred. These cases are very poorly detailed as regards the nervous signs. It is interesting to note that only three other cases of this combination of ocular and facial paralysis in diabetes have been recorded since by Schaper, Lagrange and Schmidt-Rimpler.

During the next thirty years I find only six minor references to the subject, which are mostly reports of single cases, but in 1897 Saundby writing upon diabetes in "Allbutt's System of Medicine," had evidently seen cases of bilateral paralysis of the sixth nerve, paralysis of the third nerve, ptosis, and pupillary defects. Two years later Hawthorne published further cases in the *Lancet* when describing peripheral neuritis and retinal changes in diabetes. After this there are many publications, among which the most important are an analysis of fifty-eight cases by Dieulafoy in 1905, a résumé of the published cases with references by Groenouw in 1906, and an analysis of 233 cases of ocular paralysis by Koellner in 1908.

I give here a few extracts from Groenouw's résumé for comparison with my description: paralysis of the eye muscles is not infrequently met with in diabetes; it constitutes from 4% to 7% of all the cases of eye trouble in diabetes. In Groenouw's analysis of 647 cases, 5·3% had ocular paralysis. Dieulafoy in 1905 found among fifty-eight cases paralysis of the sixth nerve thirty-five times, paralysis of the third nerve eleven times and of the fourth nerve five times, and in six cases there was paralysis of all of these nerves. Koellner in 1908 found diabetes responsible for only 1% of 233 cases of ocular paralysis examined by him. Mydriasis, sometimes associated with paralysis of accommodation, paralysis of convergence, miosis and reflex iridoplegia have been reported. Bierman, writing in 1912, is convinced that diabetes may cause reflex iridoplegia, despite Uhthoff's criticism that syphilis had not been excluded from the previously reported cases. Oculomotor paralysis may be the earliest sign of diabetes. In some cases complete recovery occurs, others improve, but do not completely recover, while in a third group the paralysis is permanent. The ocular paralysis may be associated with paralysis of other cranial nerves (I can find only facial paralysis recorded), with neuralgia of the fifth nerve with herpes ophthalmicus, neuro-paralytic keratitis, retrobulbar neuritis, frequently retinitis and cataract.

The morbid anatomy is probably a matter of hæmorrhages into the nerve trunks. Or it may be a lesion of the central nervous system of vascular origin dependent upon the diabetes, or such a lesion may be responsible both for the glycosuria and the ocular paralysis. Most writers have a leaning towards the presence of syphilis as the most likely cause of the ocular paralysis, but these all wrote at a time when the Wassermann test was not available. There are no records of histological examinations of the affected nerves. In my own fatal case I was away at the time of death and only a superficial examination of the nervous system was made; no gross lesion was present.

It seems certain, from a consideration of my cases, that syphilis is not a factor. In the one case in which the Wassermann reaction had remained positive for years the ophthalmoplegia accompanied a severe terminal glycosuria, and the rapid involvement of one oculomotor nerve after another in the course of a few days until total ophthalmoplegia was reached was unlike the development of any ophthalmoplegia which I have seen in syphilis.

Though the age incidence and the common association of degenerative vascular changes in the retina suggest a vascular pathology, neither hæmorrhage nor thrombosis in the course of the oculomotor nerves seems likely. The onset is not sufficiently sudden and the recovery is too rapid and too complete in many of the cases, to admit of such lesions. The affection of one isolated peripheral twig of

the third nerve, the symmetrical or asymmetrical involvement of one nerve on either side, and the spreading of the affection from one nerve to the others are against the occurrence of a vascular lesion. Again there are no inflammatory signs, such as pain at the time of onset and orbital tenderness. The common coincidence of retrobulbar neuritis suggests a lesion of similar nature occurring in any part of the course of the ocular motor nerves, and rarely also in the facial nerve and in the ophthalmic division of the fifth nerve.

As regards treatment, while appropriate dietetic treatment has resulted in recovery, there can be no doubt of the value of insulin in hastening a cure, and this is also true of the vascular lesions which occur in diabetes.

An apology is due for bringing forward a very old subject and for having said very little that is new. My excuse must be that no record of a series of cases and no reference to the literature of the subject have hitherto appeared in the writings of English neurologists. The series of cases with negative Wassermann reactions here recorded is of some value, and a case with recurring paralysis has not been recorded before. In conclusion, I cannot help thinking that if glycosuria were looked for in every case of ocular paralysis, cases of this type would be more commonly found.

REFERENCES.

[1] TAYLOR, E. W., in "Osler and McCrea's System of Medicine," 1920, v, 488. [2] SAUNDBY, R., in "Allbutt's System of Medicine," 1897, iii. [3] GROENOUW, A., *Handbuch d. Augenheilk.*, 3te Aufl. 1920, Abt. i, 585; *id.*, Graefe-Saemisch. *Handbuch d. Gesamten Augenheilk.*, 1904 xi, 356.

(Full references are appended to Professor Groenouw's works).

Syndromes of the Anterior Cerebral Artery.

By MACDONALD CRITCHLEY, M.D.

HILTON, in 1877, first drew attention to the constancy of the ultimate distribution of the arteries of the body, and this conception has lately been extended by Shellshear and others to the arteries of the brain. It is logical to assume that if the terminal supply of the vessels is constant, there will be uniformity in the manifestations of their occlusion. This is well illustrated in the case of the posterior inferior cerebellar artery. We have little knowledge of syndromes of the anterior inferior cerebellar artery, the internal auditory artery and the branches of the Sylvian and posterior cerebellar artery, but we believe that a similar constancy exists. We owe to Charles Foix and his pupils the foundations of our knowledge of cerebrovascular topography, and though they possibly err on the side of over-simplification, Foix has undoubtedly opened a new chapter in clinical neurology. It is to these data that I add this contribution.

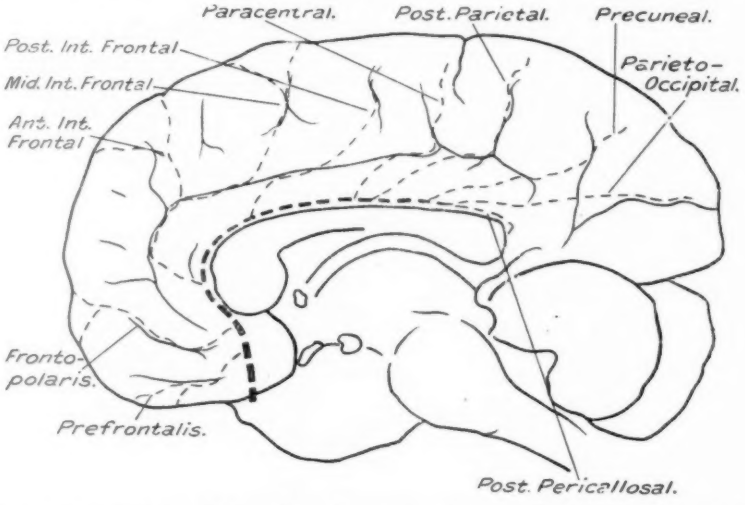
ANATOMY.

The anterior cerebral artery arises as one of the two terminal branches of the internal carotid artery. It turns forwards and inwards across the anterior perforated spot, lying between the optic nerve and the tuberculum olfactorium. At the inferomesial border of the frontal lobe, the arteries of the two sides are connected by a short anterior communicating artery. Immediately afterwards the anterior cerebral artery turns upwards and slightly forwards, and passes along the mesial surface of the hemisphere to the genu of the corpus callosum. It now follows the epicallosal sulcus and lies along the body of the corpus callosum almost to the splenium. At the junction of the anterior four-fifths and posterior one-fifth of the corpus callosum, it leaves the epicallosal sulcus and passes upwards and backwards to terminate in the parieto-occipital fissure.

Branches of the anterior cerebral artery may be classified as basal; branches from the convex aspect; those from the concave aspect; and the anterior communicating

artery. The basal branches are fine twigs which enter the anterior perforated spot, and terminate in the anterior and lower portion of the head of the caudate nucleus. One of these vessels is conspicuous on account of its size, tortuosity and important distribution. This is the recurrent artery or "artery of Heubner." It emerges from the superior aspect of the anterior cerebral artery and passes outwards and upwards to pierce the anterior perforated spot either as a single or a double vessel. Within the brain, it supplies the anterior part of the caudate, the most anterior portion of the putamen and the anterior limb of the internal capsule. Branches from the convexity of the anterior cerebral artery are the longest and most conspicuous. They vary in their mode of origin, but their ultimate area of supply is constant. These branches may be named as follows :—

(1) *Prefrontal branch*, to the medial aspect of the frontal lobe, below the sulcus subrostralis; the gyrus rectus; the olfactory peduncle and bulb; and the internal orbital convolution. (2) *Fronto-polaris branch*, supplies the mesial aspect of the frontal lobe above the sulcus subrostralis, as far forward as the pole. (3) *Anterior internal frontal branch*, terminating in the convex surface of the brain in the middle portion of the superior frontal gyrus. (4) *Middle internal frontal branch*, to the upper end of the superior frontal gyrus.



(5) *Posterior internal frontal branch*, to the uppermost end of the precentral fissure. The three internal frontal vessels frequently emerge from a common stem; the combined vessel is called the *calloso-marginal artery*. (6) *Paracentral branch* ends in the paracentral lobule, to supply the highest portion of the motor cortex. (7) *Superior parietal branches* (variable), to the uppermost part of the post-central cortex. (8) *Precuneal branch* (sometimes this is the terminal branch), to the quadrate lobule. (9) *Parieto-occipital branch*; this usually represents the termination of the anterior cerebral artery.

Branches from the concavity include twigs to the genu and body of the corpus callosum. One branch, longer and finer than the others, emerges midway between the precuneal and parieto-occipital vessels, and continues along the body as far as the splenium. This vessel—the posterior pericallosal branch—ends by inosculating with a branch from the posterior cerebral artery. There are no branches from the anterior communicating artery in man.

The territory of the anterior cerebral artery includes the whole of the medial aspect of the frontal and parietal lobes, as far back as the parieto-occipital fissure

and the subjacent white matter; genu and anterior four-fifths of the corpus callosum; the septum lucidum, anterior pillars of the fornix and part of the anterior commissure; part of the head of the caudate nucleus, the anterior part of the two outer segments of the lenticular nucleus, and the anterior half of the fore-limb of the internal capsule.

Morphological anomalies are not uncommon; according to some they are more frequent among criminals and the insane. The chief anomalies include:—The emergence of Heubner's artery from the internal carotid or Sylvian artery; A third or median anterior cerebral artery, arising from the anterior communicating artery, and passing back over the dorsum of the corpus callosum, to divide into terminal branches to the mesial aspect of both hemispheres; Absence of the anterior communicating artery with fusion of the two anterior cerebral arteries to form a single azygos artery, supplying both halves of the brain—this pattern is the rule amongst the mammalian series; Asymmetry in the calibre of the first portion of the anterior cerebral artery so that the vessel of one side supplies both hemispheres by way of a dilated anterior communicating artery; Doubling or trebling of the anterior communicating artery; Absence of the anterior communicating artery, with the persistence of two anterior cerebral arteries—this is the typical conformation among birds, amphibians and reptiles.

Syndromes of the Anterior Cerebral Artery.

It may eventually be possible to diagnose occlusion of the anterior cerebral artery at different points and to recognize the effects of thrombosis of its individual branches. At present we can only recognize the main features of disease of the anterior cerebral artery, and in particular of the branch which supplies the paracentral lobule. The frequent implication of this portion of the motor cortex and the corpus callosum accounts for several characteristic clinical features.

A crural monoplegia—or hemiplegia with crural predominance—is the result of softening of the paracentral lobule; it occurs after occlusion of the main trunk before the emergence of the paracentral artery, and also after occlusion of the paracentral artery itself. The paralysis is usually sudden, and is greatest in the distal portion of the limb; tone may be increased but is more often diminished; the knee and ankle jerks are exaggerated and the plantar response is usually extensor. There may be some sensory impairment. At times the affected limb is œdematous.

Left-sided ideo-motor apraxia occurs if the branches to the corpus callosum are implicated. If the lesion is in the right hemisphere, there may be muscular weakness as well as apraxia, in the opposite arm.

Contralateral psychomotor disorders often occur. These include, most characteristically, the phenomena of forced grasping and groping. At times, other peculiar movement-anomalies occur, such as tonic innervation, catatonia, sucking and chewing movements. Mental disturbances are common, but present no characteristic features. Aphasic speech defects are rare. At times there is a transient defect of articulation, or a tendency towards speech-iteration, but these changes are rarely constant or severe.

It is important to bear in mind, however, that in those very rare cases of occlusion of Heubner's artery (or of thrombosis of the main trunk of the anterior cerebral artery, between its origin and the emergence of the communicating artery), the fore-limb of the internal capsule may become implicated. In such cases there will be a severe degree of contralateral hemiplegia affecting particularly—in the case of occlusion of Heubner's artery alone—the face, tongue and shoulder.

Section of Obstetrics and Gynæcology.

[*January* 17, 1930.]

Three Cases of Imperforate Hymen Occurring in One Family.

By Dame Louise McIlroy, M.D., and Iris V. Ward, M.B., B.S.

Cases of imperforate vagina are not very frequently met with in gynæcological practice. The present communication is of interest owing to the condition having been found in three sisters who were otherwise perfectly normal.

G. C., aged 20, admitted to hospital in July, 1928, with a history of never having had a menstrual period. She had been quite well until six months previously, when she noticed that her abdomen was gradually increasing in size and that she had attacks of pain recurring every month. For the last two months the pain had been spasmodic and more or less continuous. For three weeks, micturition had been frequent.

On examination, the abdomen was found to contain a smooth, tense, oval swelling rising out of the pelvis and extending to about two inches above the umbilicus. There was some elasticity on palpation but no fluctuation was felt. On inspection of the vulva, the hymen was found to be imperforate and a purplish-coloured swelling was seen protruding through the vaginal aperture. The operation consisted of a circular excision of the hymen, leaving an aperture of about one inch in breadth. A considerable quantity of thick, chocolate-coloured blood began to flow from the aperture. No pressure upon the uterus was employed nor were douches used in the vagina. The cut edges of the hymen were prevented from bleeding by a continuous catgut suture. Sitz-baths were given and the discharge ceased in a day or two. The patient had no further discomfort and menstruation became regular and normal. Microscopic examination of the excised membrane showed involuntary muscle and connective tissue with a layer of squamous epithelium on both surfaces.

In July, 1929, R. C., aged 16, was admitted with a history somewhat similar to that of her sister. Pain in the back and abdomen had occurred at monthly intervals for six months. Vomiting had been present at the last attack of pain. On examination, the swelling was found to extend upwards to within an inch of the umbilicus. The upper portion was movable on the lower and was assumed to be the uterus lying upon the distended vagina. The hymen was intact, with a bluish-coloured tense projection between the labia. The operation was similar to that in the previous case. Chocolate-coloured fluid flowed from the vagina for five days. The pathological report was almost identical with the previous one. The subsequent periods were normal.

The mother of these patients said she had one other daughter, C. C., aged 14, who was well and free from pain or swelling, but who had not menstruated as yet. This girl was brought for examination and it was found that the hymen was imperforate, but that no evidence of hæmatocolpos was present. An operation was advised (July, 1929). Under anæsthesia, a swelling was felt in the lower abdomen; there was no bulging at the vaginal orifice. The hymen was excised and two pints of chocolate-coloured fluid flowed out. The contents of the vagina were more fluid than in the two earlier cases. Menstruation has been normal since the operation. The pathological report was similar to the previous reports except that the epithelial layer is not so well developed on one side of the membrane as on the other.

In none of the cases was there any atresia of the vagina or cervix. All the operations were performed under anæsthesia and no pressure or douching was employed because of the risk of sepsis. No complications followed the operations.

It may be mentioned that the condition of so-called imperforate hymen is usually imperforate vagina, due to defective canalization of the urino-genital sinus.

We are indebted to Professor Hadfield for the microscopic slides and reports, and for a photograph [1] of the second case specimen.

The Detection of the Presence of the Hormone of the Anterior Pituitary Body in the Urine as an Aid to the Diagnosis of Pregnancy.

By JOHN H. HANNAN, M.D.

(From the Physiological Laboratories of the Middlesex Hospital Medical School.)

IN 1922 Evans and Long demonstrated that intraperitoneal injections of fresh extract of the anterior lobe of the pituitary body caused a marked increase in weight of the ovaries of immature rats, and further, that large numbers of corpora lutea were formed in such ovaries.

From these experiments they concluded that the anterior pituitary body exerted a powerful stimulant effect upon the process of lutein cell formation.

In the years following 1922, this work of Evans and Long was confirmed by many observers, and the specific action of the anterior pituitary hormone on the ovaries was clearly established. In 1928 Zondek and Aschheim observed that the urine of pregnant women contained large amounts of the anterior pituitary hormone, and in a further paper published in the same year they elaborated a technique for the diagnosis of pregnancy by the detection of the anterior pituitary hormone in urine.

Their technique for the test may be summarized as follows: 1·2 c.c. to 2·4 c.c. of the urine are injected into infantile mice weighing 6 to 8 grm., in six portions, over a period of forty-eight hours. The animals are killed and examined fifty hours later. Three reactions may be found: (I) Ripening of the ovarian follicles and beginning of œstrus. (II) The production of hæmorrhagic points in the ovary. (III) The formation of corpora lutea atretica.

If the urine is from a case of pregnancy, reactions II and III, namely, the presence of hæmorrhagic points in the ovary and the formation of corpora lutea atretica, should always be present. Reaction I, however, is insufficient alone for the diagnosis, since ripening of the follicles and œstrus may be produced in conditions other than pregnancy.

Five mice are used for each test and the reaction is assumed to be positive if even only one of the animals gives a positive reaction.

Utilizing this technique, Zondek and Aschheim found that of 197 urines from pregnant women, 193 or 98% gave positive results. Of 258 controls with urines of non-pregnant women, some healthy and some with diseases of various kinds, together with the urine of four men, 254 or 99%, gave negative results. These results seemed so impressive that, at the beginning of 1929, I commenced an investigation into the value of Zondek and Aschheim's test in routine gynæcological practice with the definite intention of obtaining my material from cases which presented difficulty in diagnosis. With the coöperation of the staff of the Hospital for Women, Soho, I was able to obtain urine from such cases, and, as far as possible, I endeavoured to investigate the samples sent to me without knowing anything about their history or gynæcological findings.

At first I attempted to follow out Zondek and Aschheim's original technique, but found that two difficulties occurred which prevented me from carrying out my original intention. In the first place, I found considerable difficulty in breeding and obtaining an adequate supply of young mice of the right age, and, since five mice

[1] Shown on the screen.

were required for each test in the original technique, I had to abandon this technique after four investigations. In the second place, I lost a large number of mice from the toxic effects of the urine, especially if the sample had been kept for a day or so before injection into the animals. I therefore endeavoured to find a modified technique which would use a smaller number of animals and would employ animals which could survive the ordeal of the injection of the urine.

After some preliminary work, largely by the old method of trial and error, I developed the following technique: One albino rat only is used for each test, aged six to eight weeks: 3 c.c. of the suspected urine are injected subcutaneously in one dose, and the animal is killed and examined ninety-six hours later.

A positive reaction consists of the presence of hæmorrhagic points in the ovary, representing hæmorrhages into the follicles, which are easily detected by the naked eye. In compiling my results I have omitted two groups of cases: (1) Those of my early experiments when I was developing my technique. (2) Those women who, after missing one or more periods, had a loss, since it is clear that unless something can be produced by these women for examination, it is impossible to ascertain definitely whether the result of a test, in such instances, is accurate or not.

There is no mention, by other observers, of this difficulty, which occurred with considerable frequency in my series.

The following tables show my results after utilizing the uniform technique which I have outlined.

A.

Normal Pregnancy		
6 weeks to 3 months	21 cases	2 wrong
3 months to term	12 ,, ...	1 ,,
Total ...	33 ,, ...	3 ,,
Ectopic Pregnancy		
Tubal abortion	2 cases	both positive
Tubal mole	1 case	negative
Pelvic hæmatocele	2 cases	both negative
Total ectopic pregnancies ...	5 cases	

A fœtus was found only in the case of both tubal abortions.

B.

Puerperium

3 cases; daily tests. Two women ceased to give positive results on the fifth day after delivery; one woman ceased on the seventh day.

Total of all pregnancies 41; 3 wrong ... (error 7·3 %)

C.

CONTROLS.

Normal Women		
Regular menstrual cycles ...	15 cases	0 wrong
Secondary Amenorrhœas		
Probably endocrine in origin ...	8 ,, ...	2 ,,
Menopause		
With amenorrhœa	12 ,, ...	4 ,,
Fibroids	8 ,, ...	2 ,,
Ovarian Cysts	3 ,, ...	0 ,,
Genital Carcinoma	7 ,, ...	2 ,,
Exophthalmic Goitre	4 ,, ...	2 ,,
Men ...	5 cases ...	2 positives

D.

SUMMARY OF RESULTS.

Pregnancy	41 ...	3 wrong ...	(represents 7·3% error)
Normal women ...	15 ...	0 ,, ...	(,, no error)
Women with disease	42 ...	12 ,, ...	(,, 28% error)

A consideration of my results justifies the following conclusions:—

(1) Zondek and Aschheim's finding that the urine of pregnant women contains large amounts of the anterior pituitary hormone is confirmed.

(2) The presence of the fœtus is the essential factor in the production of this phenomenon, since the reaction quickly disappears in the puerperium and is not found in cases of ectopic pregnancy where the fœtus has perished.

(3) Normal women, with regular menstrual cycles, invariably give a negative reaction.

(4) Women with diseases of various kinds, particularly those with a disturbance of the endocrine balance, pass urine which, in many instances, contains the anterior pituitary hormone.

As a further contribution to this subject I have analysed the results of other observers who have utilized the original Zondek-Aschheim technique.

The following, in tabular form, represents these results.

CASES RECORDED BY LOURIA AND ROSENWEIG, BRÜHL, ASCHHEIM AND ZONDEK, VOZZA.

Total	913			
Pregnant women	452	...	8 wrong	(represents 1·8% error)
Non-pregnant women	461	...	15 ,,	,, 3·2% ,,

In endeavouring to pass an opinion on the clinical value of the Zondek-Aschheim test, I propose to consider the combined figures of Zondek-Aschheim tests by other observers as compared with my own.

A study of these figures will show that, so far as non-pregnant normal women are concerned, my figures and those of other observers are in agreement.

With regard to pregnant women, it will be seen that my percentage of error is higher than that of other observers.

With regard to women with disease, my percentage error is very much higher than that of other observers. I would like to point out, however, that apart from the different technique which I have employed, my series consisted of cases which simulated pregnancy and were usually associated with amenorrhœa, whereas the cases recorded by other observers were chosen at random. The figures of other observers, however, are very impressive and cannot be lightly dismissed.

In my series of pregnant women I have not counted, as positive, any in which there was the slightest doubt about the reaction, but I have no doubt that my percentage of error could be reduced by taking serial sections of the ovaries, when the characteristic changes in the follicles could be found even where they were not visible to the naked eye.

Turning to my control series, further work, using rats a week or so younger, might improve these figures, since an essential feature of the test is the production of changes in the ovaries of animals just before they reach maturity.

Long and Evans state that œstrus commences in the albino rat on about the 77th day (range recorded 45th-147th day). It is possible that my figures might be improved by using rats 4-6 weeks old rather than 6-8 weeks, since a consideration of the possible range shows that, in some instances, rats may have been used which were mature at the time of test.

My finding that certain urines are very toxic to the animals used in the tests is confirmed by these observers—a mortality figure of between 10% and 20% being recorded even when preservatives are added to the urines.

In my series, I have found that the urine of pregnant women is much more toxic to rats than the urine of non-pregnant women. As I have shown, the test is positive only when the ovum is still alive. Vozza and others have shown that the reaction is positive in cases of vesicular mole in which no fœtal remains are perceptible. I have only had an opportunity of confirming this during the past week, having observed one case of this condition during this time.

If these findings are confirmed, then we may take it that overaction of the anterior pituitary is due to the hormonic stimulus derived not from the fœtus but from the chorion.

There can be little doubt that further work will reduce the percentage error of these tests considerably, but certain facts remain for consideration. In the first place we have so many variable factors—we have the age and weight of the animals used, the amount of urine injected, the varying sensitiveness of the animals, the varying amount of the autacoid present in different women at different periods of pregnancy—so that the test is hardly likely to develop into a specific one.

After all, it is only in the early cases of pregnancy that we should require the assistance of a test.

If such a test, however, should be associated with the smallest percentage of error, then it is better for our reputations if we continue to rely upon the old method of seeing the patient again in a month's time.

In conclusion, although I feel some disappointment in adding this test to the long list of tests for pregnancy which have arisen in the past and which have not proved specific, I am compensated by the knowledge that the anterior pituitary body has an important place in the complex mechanism concerned in the function of reproduction, and feel that further research along these lines will, probably, prove a fruitful one.

Discussion.—Dr. EDWIN ROBERTSON: So far, 400 of the 700 tests made in 1929 at the Pregnancy Diagnosis Station have been controlled. In eleven negative and one positive cases our diagnosis was labelled "incorrect." This positive case showed evidence of endocrine dysfunction: in five cases we had no details and were just notified that we were incorrect; in five there was evidence in the history of fœtal death having taken place before the mother's urine was sent for testing, and in one case, that of a definitely pregnant woman, we gave a negative result, but on receiving a second specimen for testing, we gave a positive result.

Dr. Hannan has said that in a few days after fœtal death, just as at the end of a full-time pregnancy, the urine becomes negative; that, I think is, in a measure, borne out by five of our "incorrect" series. We have found that, in an incomplete abortion for example, so long as there are active placental elements present, the urine will give a positive reaction; and this is borne out in such cases as hydatidiform mole and chorion-epithelioma, both of which we have tested and found positive. In one case of chorion-epithelioma in which a year ago the uterus and appendages were removed, and which now shows metastasis in the lungs, a positive result was obtained a short time ago.

Therefore, of these twelve cases, five findings were probably not really incorrect, for it must now be understood that the test is only positive when active products of conception are present.

Dr. F. DICKENS (introduced by Mr. L. CARNAC RIVETT): Dr. Hannan's paper has been of special interest to me as Dr. Allan and myself have for the past eighteen months been testing the original Zondek-Aschheim reaction in the Courtauld Institute of Biochemistry at the Middlesex Hospital. Our results, unlike those reported by Dr. Hannan when using his own modification of the test, are on the whole very satisfactory for a reaction of this kind. For example, we compared a number of early cases of pregnancy with specimens from non-pregnant women, normal and otherwise. The clinical diagnosis was unknown to us until after the completion of the experiment. In 125 cases of definitely pregnant women, 122 results were positive and 4 negative; the error was thus 3·2%. Similarly, of the total of 82 definitely non-pregnant women, only one—a woman at the menopause—gave a positive result (error 1·2%). This was the most disturbing contrary result yet obtained. The result in 5 other cases at the menopause was negative, and Zondek-Aschheim quote a large number of satisfactory negative results in this condition. Of the 4 negative exceptions among pregnant women, one miscarried three weeks after the test. The remaining 3 proceeded to term normally and the test must therefore be regarded as definitely in error in these.

The test is positive very early in pregnancy. Thus in one case, in which the onset of the menstrual period was only nine days overdue, the test was intensely positive. This early diagnosis certainly constitutes one of the most valuable points of the test. The reaction is negative very soon after the maternal and fœtal connection is severed, e.g., 48 hours after delivery and four days after abortion the test was negative. During lactation and menstruation the test is also negative. One case of pituitary tumour examined gave a negative result.

The above results have been quoted rather fully as they differ clearly from those of Dr. Hannan. The reason appears to me to lie in his use of the rat instead of the mouse as used in the original test. In the mouse of the age used, spontaneous luteinization is rarely or never found; the same is probably not true of rats of the age used by Dr. Hannan. A false positive result would be obtained in an animal in which spontaneous luteinization occurred. Also mice may be procured in large numbers from a dealer and the age checked with sufficient accuracy by weighing. Mice are cheaper than rats and the death-rate, though high (it may be up to 20%), is not serious if five mice are used, though by using only one rat this mortality is liable to cause much trouble. Serial sections of the ovary in the mouse are only necessary in very exceptional cases—perhaps in only 1% roughly. Therefore, there seems little reason for abandoning the mouse in favour of the rat in this test, which, although, as has been shown, it is not absolutely infallible, is yet, in my opinion, the most satisfactory test for pregnancy hitherto described, and has the peculiar virtue of giving good results in early cases.

Dr. B. P. WIESNER said: The Zondek-Aschheim test for pregnancy should be judged only on the basis of sufficient material collected under clinical conditions and tested according to the original methods. These three conditions have been fulfilled in the pregnancy diagnosis station, which was established in the Animal Genetics Department (Animal Breeding Research Department) last year. The test was carried out on a large number of urines sent by practitioners and hospitals from all parts of Great Britain and Ireland, and was found to be satisfactory, there being only a real error of little more than 2%. This is true, however, only if it is carried out without reducing the number of mice employed, or substituting the rat for the mouse. One could hardly call the test the Zondek-Aschheim test if such alterations were made.

The only modification adopted by the pregnancy diagnosis station was the abandonment of microscopical examination of the ovaries, which was found to be unnecessary. The test had to be quick to be of any use. As the results show, the test is of very definite use and represents a further addition to the means of differential diagnosis of pregnancy. It permits diagnosis very early in pregnancy. It is not correct to say that the test is based on the occurrence of "the" anterior lobe hormone in the urine, since the anterior lobe of the pituitary contains at least four hormones, as shown by recent work in Edinburgh. Only two of them influence the ovary, and are elaborated by the human placenta. Their appearance in the urine causes the effect described by the originators of the test and is a sign of placental activity, not of the presence of a fœtus. Thus the test is not a pregnancy test, *sensu strictu*, and it is to be hoped that a chemical test for the presence of a living fœtus will be elaborated.

Dr. VOGE (Edinburgh) said: To the chemist the mechanism whereby sexual precocity of immature mice is brought about is the interesting phenomenon underlying the Zondek-Aschheim test. In a letter to the *British Medical Journal*, November 2, 1929, a chemical test was described, based upon the assumption that a compound of the iminazolyl type is responsible for this phenomenon. The test employed is the addition of bromine water (saturated solution) to the urine under examination; a positive reaction, associated with pregnancy, is indicated by the development of an orange-pink, or pink, colour on boiling. As originally described by Knoop, this test is specific for histidine or histamine, and in fact the addition of 0·12 to 0·06% of the former substance to a normal urine causes it to simulate (as regards this chemical test) a urine from a pregnant female. The addition of xanthine, hypoxanthine, alloxan, alloxantin, caffeine, arginine, and urea to normal urine does not cause it to alter in its behaviour to bromine water.

The cases then reported on have been considerably extended, 643 urines having been examined. These are divided into the following groups:—

Group A.—Bromine water test correlated with Zondek-Aschheim test. 326 urines were examined and an agreement of 91% is recorded (11 consecutive and similar errors are neglected since in these the test was performed upon five-week-old urines, and this fact appears to be the source of error).

Group B.—Bromine water test correlated with clinical history.

(I) *Undoubted Pregnancy.*—117 urines from such cases were examined, the varying period of pregnancy being from six weeks to full term. 94·9% agreement is obtained. It may be noted that urine from such a case may remain positive for three to five days after delivery, thereafter returning to negative.

(II) *Non-pregnant Females.*—100 urines have been examined from such cases, and in 98% a negative test was recorded.

(III) *Males.*—The urine of 100 males has been examined, and in 96 cases a negative reading was found to occur. The exceptions are cases with pleurisy and pericarditis with effusion.

It is realized that the percentage of successes with the Zondek-Aschheim test is higher, but this test is put forward with a dual object in view. Firstly, it is cheap, quick, and simple; and secondly, it may open up a line of investigation with the mechanism of this interesting and valuable reaction. It is specially on account of this latter that this work is now advanced. I wish to acknowledge the coöperation and help of Dr. John Young, of Edinburgh, who has carried out a considerable number of these tests and supplied material and clinical histories.

Mr. H. BURT-WHITE said: At St. Bartholomew's Hospital Dr. Archer and I have investigated the "bromine water test" for pregnancy. The patients whose urines have been examined fall in three groups.

(1) *Pregnant Women* (245).—A positive reaction was obtained in all except 22 cases, that is, there was a 9% error. The earliest positive reaction was obtained in a six weeks' gestation. In those cases in which the test failed, the urine was very dilute, concentrated or infected.

(2) *Women, not Pregnant.*—In this group, not a sufficiently large number of normal women was investigated:—

	Cases	Positive reaction
Exophthalmic goitre ...	6	5
Pituitary tumour	1	0
Various conditions ...	9	1
Malignant disease	4	4

It is apparent that in this group of 20 cases there was a 50% error.

(3) *Males.*

	Cases	Positive reaction
Various conditions ...	10 ...	2 cases { (1) Diabetes mellitus (2) Carcinoma of colon
Normal	7 ...	—

Mr. L. C. RIVETT said he could not congratulate Dr. Hannan on having evolved a technique which allowed a much larger percentage of error than the original test.

The clinical diagnosis was easy in at least 99% of cases, and of the doubtful 1 per cent. very few presented real difficulties to the expert. Unless a test could be evolved which improved on this, it was not of practical value.

Dr. HANNAN (in reply) said he had been interested in the figures brought forward by the speakers in discussion. It was clear, however, both from these and from those which he had considered in his paper, that a percentage error of at least 3% must be expected, even when the original Zondek-Aschheim technique was adhered to. He was not altogether satisfied that his own unfavourable figures were entirely due to the difference in technique employed, since the most unfavourable part of his series consisted of cases of amenorrhœa which simulated pregnancy, whereas the controls put forward by the other speakers did not.

The weak part of the Zondek-Aschheim test was the number of animals employed, and although the percentage error could be reduced by using a large number of animals, it did not seem possible to exclude the possibility of error even if an uneconomic number of animals were used for each test.

In his view, a test for pregnancy must prove absolutety reliable if it was to serve any useful purpose. He did not intend to employ this test, therefore, as a routine, although he proposed to undertake a limited number of tests, using large numbers of mice for the purpose of research.

Further Studies in Osteomalacia.

By J. PRESTON MAXWELL, M.D., F.R.C.S.

(*Professor of Obstetrics and Gynæcology, Peiping (Peking) Union Medical College.*)

OSTEOMALACIA is a disease which exerts its evil effects on the process of reproduction. When conditions are such that it becomes widespread through a nation or an isolated colony, it may hinder the reproduction of a race, and so influence the course of history. Researches into the causes of extinction of the

Norse colony which was founded by Eric the Red in A.D. 985 at Herjolfsnes, Greenland, afford an interesting field for speculation in this respect. The last survivor of this colony died about the end of the fifteenth century. Excavations there have revealed a number of skeletal remains, which have been carefully studied by Professor F. C. C. Hansen, of Copenhagen. The female skeletons are those of young women only; in the two cases in which the details of the pelvis are available the findings are most instructive. In one (No. II) the skeleton of a woman aged from 25 to 30, the pelvis is asymmetric and belongs to the flat rachitic type, and the spine shows a moderate scoliosis. The other (No. I) belonged to a woman aged between 30 and 40. The pelvis is asymmetrical and kyphotic, the lower aperture is contracted and kypho-scoliosis is also present. A more detailed examination of this pelvis reveals the following interesting features.

The upper measurements are normal, therefore there is no general contraction. The transischial measurement is only 8 cm., instead of the normal 11 cm. The sacrum is beginning to curve forward and the index sacralis is shortened, and there is a definite bend at the junction of the descending ramus of the pubes and ascending ramus of the ischium, similar to that which occurs in osteomalacia. From the photographs, the kypho-scoliosis strongly suggests an osteomalacic rather than a tuberculous disorder.

The fact that the skeletal deformities in the first case are distinctly of rachitic origin, together with the fact that rickets and osteomalacia are identical in ætiology, has led me to believe that the deformity presented by the skeleton of the older woman may have been the result of osteomalacia, and that rickets and osteomalacia played their part—possibly a most important one—in the extinction of the Herjolfsnes colony.

The rise of the incidence of osteomalacia in Shansi affords another interesting field for speculation. Shansi was visited by a severe famine in 1875. Coincidently with this disaster, and partly preceding it, there was an immense increase in the growth of the poppy and the use of opium, so that for a time Shansi was the province of the whole Empire most cursed by this habit. The effect on the province was twofold: first, an increase in the incidence of osteomalacia, and secondly, a weakening of the physique and morale of the people of a whole generation, and it is only within recent years that the Shansi people have again begun to take their proper place in regard to physique amongst the Chinese.

During the present famine, 1928-29, large numbers of women and girls of marriageable age have been drifting into Shansi; seventeen thousand are said to have passed through Yen-men-kuan. The peculiarity of this influx is that these women and girls are being distributed over the countryside and not drafted into the large cities. It is clear that the greater part of the influx is not for vicious purposes, but is more probably due to the havoc which osteomalacia has played amongst the women of marriageable age during the last twenty-five years.

Ætiology.—One of the most interesting phases of the osteomalacia problem concerns its relation to rickets and late rickets. To my mind they represent merely different manifestations of the same disease. This being so, we should be able occasionally to trace the effect on both mother and child. Hamilton has stated that normally a store of calcium is built up in the fœtus, especially in the last three months. If this is so, the child born from a mother with osteomalacia starts life handicapped by being unable to make up its calcium store to the proper figure, owing to an insufficient supply of calcium during the last few months of pregnancy. Should this be true, and if during lactation the supply is also short, it is very likely that there will be an early manifestation of rickets in the child.

In a former paper we mentioned the case of a baby born of a mother with active osteomalacia who had developed some signs of rickets a few months after birth. Dunham has published another case. For the following third case I am indebted to Dr. J. R. B. Branch, of the Hunan Yale Hospital, Changsha.

Mrs. C. S. W., aged 28, was admitted to the Hunan Yale Hospital suffering from osteomalacia. She had had two children. The first died at the age of 3 months from some unknown cause. About six months after the birth of the second child, whilst still carrying on suckling, she began to suffer from the characteristic pains of osteomalacia. She came to hospital after being ill three and a half years. The case was a typical one of osteomalacia; the characteristic deformity of the pelvis was present, and the interischial diameter was reduced to 5 cm. Under cod-liver oil and calcium phosphate and sunshine, she made a complete recovery, except for the deformity. At the same time this second child, S. O. W., was admitted to the hospital. She was suffering from pain in the shoulders and had been unable to walk for the past eight months. She had been suckled for a year, and began to walk at the age of two.

She presented typical rickets with the rachitic rosary, affection of the epiphyseal ends of the radius and ulna on both sides, curvature of the spine and bow legs. Under the X-ray there was rarefaction of all the bones of the pelvis and typical changes in the radius and ulna. Under antirachitic treatment, combined with osteotomy of the right tibia and manual reduction of deformity of the left leg, she was much better after three months' treatment, but apparently some flattening of the pelvis had already taken place, if one may take the X-ray of the pelvis as a criterion.

In this case osteomalacia in the mother and rickets in the child developed at the same time.

Proof of the existence of antenatal rickets in the fœtus, associated with active osteomalacia in the mother, would furnish even more conclusive evidence of the relation between the two diseases, and this proof I am now fortunate enough to be able to present.

It is true that Kassowitz has published illustrations of the bones of new-born children which seem almost conclusive of the existence of antenatal rickets, though Schmorl is not satisfied as to the evidence, and Korenchevsky leaves the question an open one.

In our preceding paper, Dr. Miles and myself stated that, although the child may suffer as a result of the calcium shortage, we had been unable to find actual evidence of antenatal rickets. That evidence I am now able to supply. In the end of December, 1927, a woman came into the Ping-ting-chow Hospital suffering from active osteomalacia with a severe deformity of the pelvis. Cæsarean section was performed by Dr. Hsü Teh Hui, and a living child was obtained, but it died after four days, with curious patchy œdema and hardening of the muscles, possibly sclerema neonatorum. This child, on examination, was proved indisputably to have suffered from antenatal rickets.

Not only is the radiographic evidence quite clear, but sections of the bones showed the characteristic alterations in the cartilage at the line of growth, though the production of osteoid material is very poor, possibly due to practical cessation of growth in an ill-nourished fœtus.[1]

Since this specimen was obtained I have had another case of a child, born from a mother suffering from prolonged mild osteomalacia, which presented at birth clear radiographical evidence of fœtal rickets. Five weeks after birth—the mother having been treated with cod-liver oil and irradiated ergosterol in the meantime—radiography showed that the disease was practically healed.

These cases amply justify the conclusion that osteomalacia and rickets are one and the same disease. The same food and environment produce, in patients whose bones have reached maturity, osteomalacia; in those whose bones are still in the developmental stage, rickets.

Another interesting fact is that Dr. J. Hammond, of Yale, formerly working in the Peiping Union Medical College Hospital, informs me that in his inquiries into rickets in the north of China, he found that the disease in the regions affected by

1 Since this paragraph was written, Professor Hubert Turnbull, of the Bernhard Baron Institute of Pathology, has kindly examined my slides, and he pronounces the case to be one of fœtal rickets plus infantile scurvy (Barlow's disease). A full report of this case will be published in the near future.

osteomalacia, was of a more severe type than that found in the region around Peiping, where osteomalacia is of only occasional appearance.

Deformities due to the Disease.—In osteomalacia there are three main classes of deformity, those of the spine and chest, those of the pelvis, and those of the long bones.

(1) Deformities of the spine and chest.—There are two distinct varieties of spinal deformity. In the first variety, the usual one, there is not merely a kyphosis but also a scoliosis with some rotation.

The second variety, which is very rare, is characterized by pure kyphosis. I know of only two such cases; one in a patient who has been under my care at the Peking Union Medical College, and the other in a dry specimen, history unknown, in the Museum of St. Bartholomew's Hospital, London.

The particulars of the patient under my care (figs. 1-3) are as follows:—

Mrs. L. C., aged 37 (Hospital No. 18,564), had never been out of Peking.

History.—In the fifth month of her fourth pregnancy, in 1925, she began gradually to have pain in the back and thighs. Since April, 1926, she has been unable to walk or sit up without

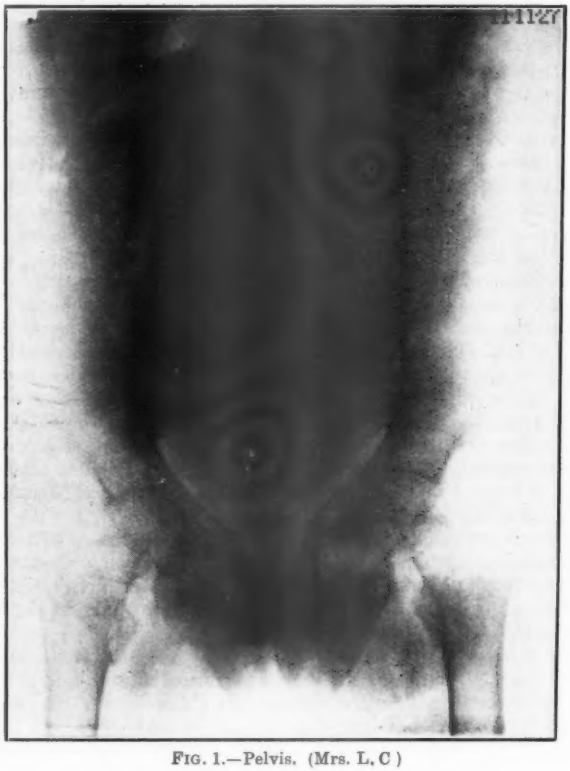


FIG. 1.—Pelvis. (Mrs. L. C.)

help. For the last year and a half she has kept the knees and thighs flexed. For the last four months there has been some pain on movement of the arms. Patient has noticed that her sitting height was diminishing. Has never had "ma-mu" (numbness of the hands and

arms) or tetany. Her meals have been two a day—Breakfast: Corn bread and a bowl of soup containing cabbage. Supper: Two bowls of rice or millet "chow" and a little salted vegetable. No meat, fish or bean. She has been on this diet more or less for ten years.

Pregnancies		Age	Remarks
First pregnancy	...	27 ...	child died aged 1 year, from diarrhœa
Second	,, ...	28 ...	child living and well, 9 years old
Third	,, ...	30 ...	child living and well, 6 years old
Fourth	,, ...	35 ...	child died aged 1 year, from diarrhœa

All were easy labours.

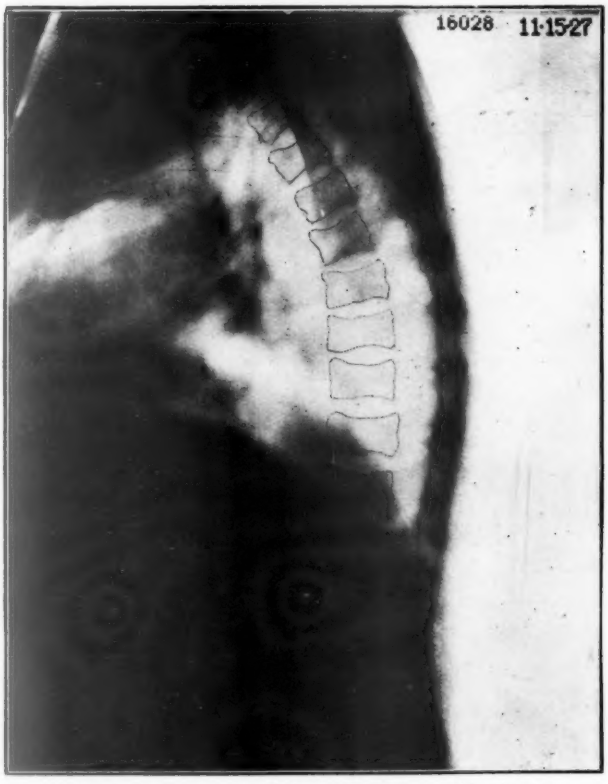


FIG. 2.—Chest at commencement of treatment. (Mrs. L. C.)

Patient's blood-calcium on admission averaged 10·8 mgm., phosphorus 3·6 mgm.

Wassermann reaction, negative.

Chest.—Costal margins flared, with typical tenderness, especially in spots along the ribs.

Nervous System.—No sign of involvement except an irritability of the neuromuscular system. The electric irritability of the nerves and muscles of the right arm and leg (those tested) was definitely increased, the face remaining normal; within a fortnight, under treatment, this condition had returned to the normal.

Pelvic Measurements.—Interspinous 21·5 cm., intercristal 26·0 cm., external conjugate 18·0 cm., interischial 5·0 cm.

Pelvis markedly rostrated.

On admission any movement resulted in pain and she preferred to lie on her side with the knees drawn up. The uterus showed a four-and-a-half to five months' pregnancy, and the last monthly period had been on May 19, 1927. X-ray examination showed a typical osteomalacic pelvis. On this occasion, antero-posterior films only were taken and no deformity of the spine was noticed.

On examination, however, from the lateral aspect, a slight anterior bowing of the entire thoracic column was evident. The lumbar column was slightly straighter than usual, and the sacrum was definitely bent, forming almost a right angle with the apex at about mid-sacrum. After treatment with cod-liver oil and calcium, ultra-violet light, and massage,

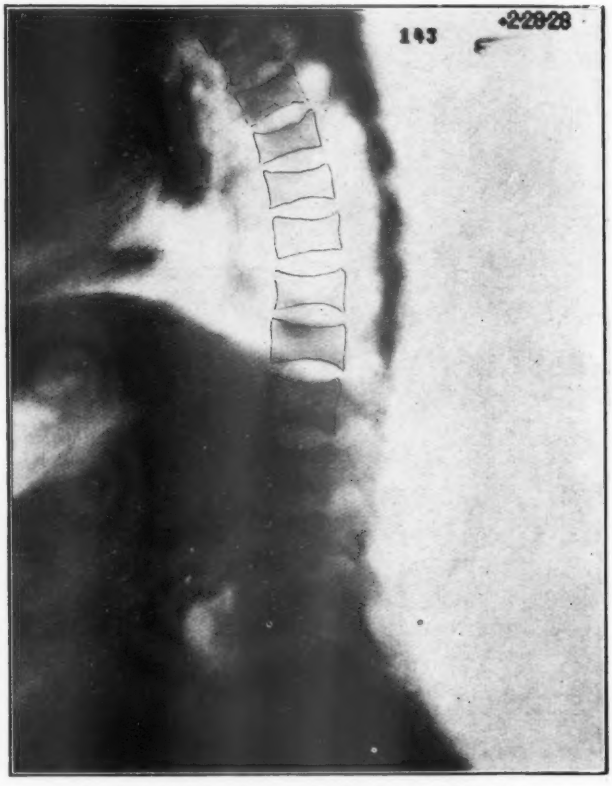


FIG. 3.—Chest after two months' treatment. (Mrs. L. C.)

the spine was re-examined on February 28, 1928, roughly three and a half months after admission, and the X-ray report was as follows: "There seems to be some increase in the lumbar lordosis"—and by this time the Cæsarean section had been performed—"and some straightening of the thoracic curvature"; and it can be seen that this straightening is marked when the two skiagrams are compared. She left hospital much improved, the Cæsarean section wound having healed in a normal way. A year later she was well. Calcium 10·8 per 100 c.c. serum; phosphorus 2·5 per 100 c.c. No treatment during this year. Estimated increase in height after treatment was 4 cm.

As an example of the more common spinal deformity I give the details of another case (figs. 4-6).

Mrs. S. T. K., a Chinese woman aged 29 (Hosp. No. 19786), was admitted to hospital with the following history.

She has been unable to walk for two years, and there have been dull aching pains in the thighs and lumbar region for nine years, which started during lactation one year after the birth of her only child. She has had the typical adduction of the thighs with painful spasm of the thigh-muscles, and during the last four years the chest has become deformed.

Her meals have been almost identical with those of the patient given above, and she has been in the house almost continuously for five years.

Pelvic measurements: Interspinous 21 cm., intercristal 24 cm., external conjugate 17·5 cm., interischial 7 cm., pelvis markedly rostrated.

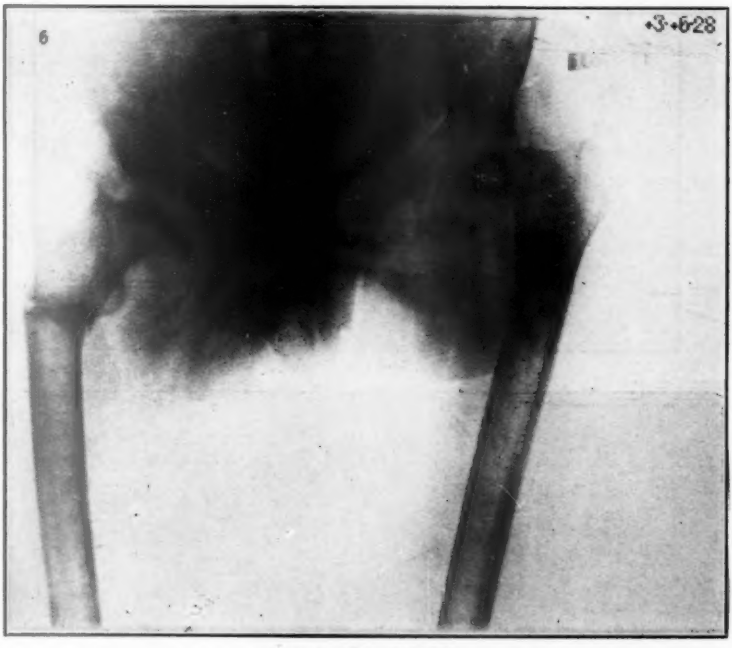


FIG. 4.—(Mrs. S. T. K.)

Blood and urine normal except for some anæmia. Wassermann reaction negative; calcium 6·6 mgm. per 100 c.c. serum, phosphorus 2·8 mgm., diffusible calcium 4·1, non-diffusible calcium 2·5, albumin 4%, globulin 2·6%.

Under treatment with cod-liver oil and calcium the total calcium rose in three weeks to 8·2 mgm., and the phosphorus to 4 mgm., whilst the diffusible calcium remained constant.

The patient has never suffered from tetany. The dorsal spine showed a marked S-shaped scoliosis. There were multiple fractures of the first ribs, both fourth ribs near spine, the right fifth rib, the right sixth rib in the axilla and probably the eighth and ninth, and the axillary border of the right scapula. In the pelvis the right pubic bone and right ischium show fractures. The left ischium is fractured and the right femur is fractured just below the lesser trochanter, whilst the necks of both femora show marked coxa vara.

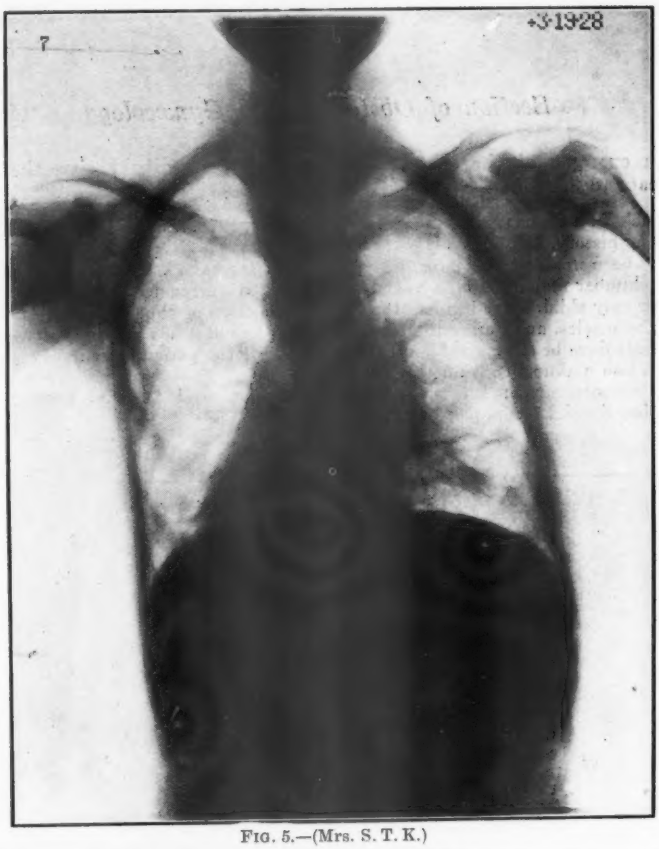


FIG. 5.—(Mrs. S. T. K.)

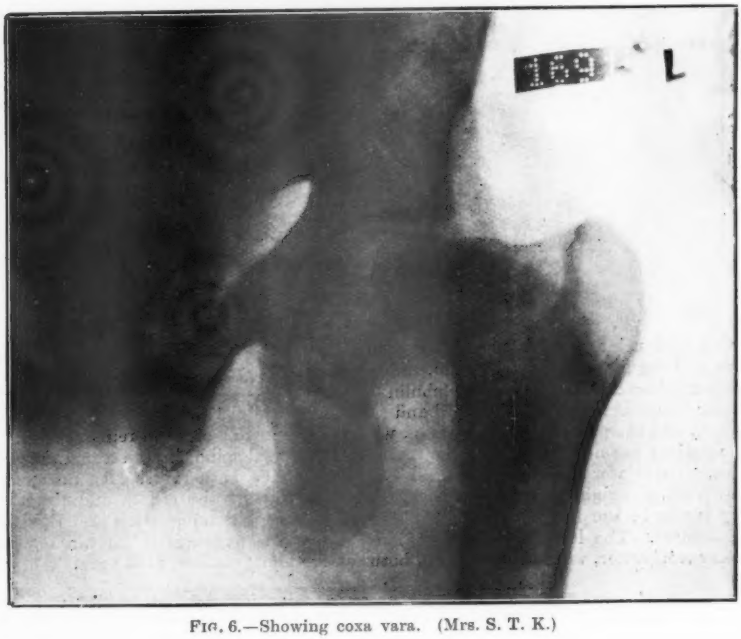


FIG. 6.—Showing coxa vara. (Mrs. S. T. K.)

In contrast with these two cases I will quote a third which presents somewhat different features (fig. 7.)

Mrs. K. T. C., a Chinese woman, aged 24 (Hosp. No. 22523), who had never been pregnant, was admitted to hospital on December 7, 1928, suffering from pain in the thighs and lumbar region, and difficulty of walking. This trouble had been gradually coming on for the last four years, and had been worse during the last two years. She had noticed bending of the spine and shortening of height.

She presented typical osteomalacia. The thighs were adducted and rotated inwards, and the spasm of the adductors was so severe that the legs could not be separated for a proper vaginal examination. She had never had tetany. The lower cervical and upper lumbar spine presented a moderate kyphotic curve, with a trace of scoliosis beginning. She had had a diet closely approximating to that described in the first case, had been living in narrow quarters, and rarely left the house.

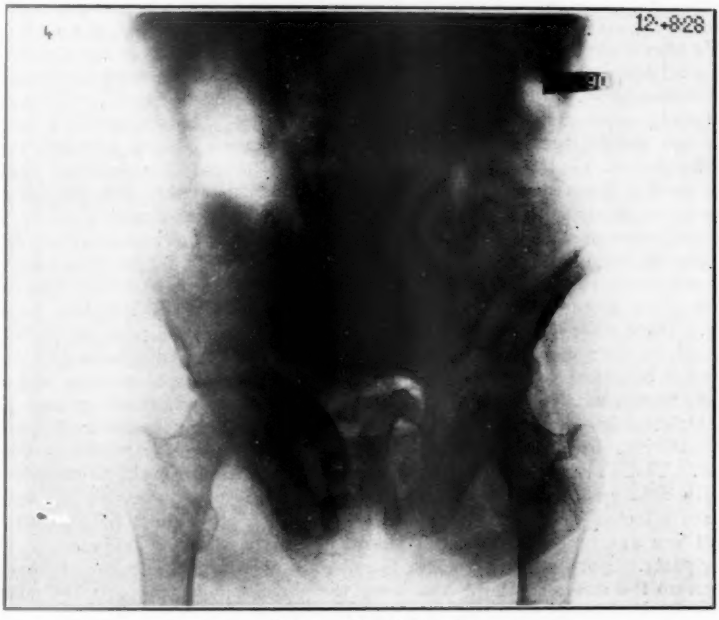


FIG. 7.—(Mrs. K. T. C.)

Her pelvic measurements were as follows: Interspinous 19 cm., intercristal 24 cm., but pelvis rostrated, external conjugate 18·5 cm., interischial 3 cm., a finger could not be brought down between the ischial tuberosities. The blood and urine were normal, and the Wassermann reaction was negative.

On Admission.—The blood-calcium was 7·5 mgm. per 100 c.c. of serum and the blood-phosphorus 4 mgm.

Three weeks after admission the calcium had risen to 8·6 mgm., and the phosphorus had fallen to 3 mgm.

On discharge (January 30, 1929) the calcium had risen to 9·9 mgm. and the phosphorus to 5 mgm. whilst the patient had lost the pain and the spasm of the adductors and was able to walk well, separate her legs, and rotate the thighs outwards.

The treatment was cod-liver oil 15 c.c. t.i.d., calcium lactate 1 grm. bis die, and irradiated ergosterol 0·00015 mgm. once a day, combined with ultra-violet light exposures and massage.

It will be noted that the first case shows an onset after several pregnancies, the second an onset during the first lactation, the third an onset in a woman who had never been pregnant.

(2) Deformities of the Pelvis.—At first sight one might think that there was no rhyme or reason about the deformities of the pelvis, as often the crushing up of the bones so distorts the pelvic girdle as to make it shapeless, but this is not the case. There are three main deformities which characterize an osteomalacia pelvis when fully developed. These are rostration, approach of the ischial tuberosities to one another, and an increase in the concavity of the sacrum with a tendency for the lower end to come forward. In speaking later on of a commencing case of osteomalacia I note that it was specially observed that rarefaction was taking place adjacent to the pubic symphysis. It will be found that the points where the pelvic girdle yields are especially the pubo-iliac junction and the ischio-pubic junction. The yielding of the former gives one the rostration, the yielding of the latter gives one the approach of the ischial tuberosities. The presence of the os acetabuli probably also contributes to the weakness of the union at this point.

How far the deformity is due to pressure from without, and how far to muscular action, is not clear, probably both forces contribute to the result. No doubt the cross-legged position assumed in sitting on the "kang"[1] has something to do with the marked deformity in our cases, for the resistance of the adductors to the outward rotation of the thigh so caused must thrust the head of the femur forcibly against the weakest part of the acetabulum. Probably the sitting posture also tends to produce the crumpling up of the sacrum, and with the approach of the ischial tuberosities to one another, the ischio-pubic ramus often becomes curiously deformed, due to the yielding of the ischio-pubic junction. A further characteristic deformity in many of these cases is the rolling in of the iliac crest, so that the iliac fossa tends to become narrow and deep rather than broad and shallow. Once these deformities have occurred it seems impossible to bring the bones back to the normal, hence the increased need for early diagnosis and arrest of the disease before these bendings have occurred. Fracture occasionally occurs in the pelvic bones, but it is much less common in these than in the long bones.

(3) Deformities of the Long Bones.—There are two principal deformities of the long bones, i.e., bending and fracture. It is difficult to say which is the more common. There are many cases of osteomalacia in which the chest and the pelvis are badly deformed, and in which the long bones seem to escape; but where the latter are affected it is very rare for the pelvis or the chest or both to escape. Where there are multiple fractures there is nearly always evidence of bending in other parts. For instance in Case II not only are there a number of fractures of bone, but on the one side there has been the development of a marked coxa vara. Occasionally there is much bending with little fracture; why, I am at present unable to state.

These cases bring up a further question, that of the relation of osteomalacia, spasm of the adductors, and tetany, to the calcium and phosphorus content of the blood.

Osteomalacia, like rickets, is most erratic in the matter of fractures and bending of the bones. The first and the third cases exhibit no fractures, whereas the second case gives evidence of numerous ones. In the second case a woman with osteomalacia presented a low serum calcium of 6·6 mgm. per 100 c.c., but she had never had tetany, and in the first case the serum calcium on admission was 10·5 mgm. per 100 c.c. and yet there was distinct irritability of the muscles, verging on tetany. Further, the latter suffered far more from the pains of osteomalacia than did the former, whose osteoporosis was more marked. To attempt to explain these differences in the present unsettled state of our knowledge concerning the forms in which calcium exists in the body—and more particularly in the blood—becomes a matter largely of speculation.

[1] The heated platform found in Chinese houses in the north.

Certainly much evidence has accumulated during recent years which indicates that not all of the calcium of the blood exists in the form of simple calcium ions. We are beginning to talk rather glibly of diffusible and non-diffusible fractions, of ionizable and non-ionizable calcium, and some assume that these two expressions mean the same thing. Data are being collected which for the time may offer practical help with our problems and make us aware of the complexity of the reactions involved, but we must continually have in mind the danger of drawing conclusions until a chemically sound basis has been provided for the observations recorded. To the best of our present knowledge, muscle irritability depends rather on the calcium-ion concentration than on the total calcium content of the blood. In the cases here considered we know nothing of the actual calcium-ion concentration, but it is possible that the second patient failed to exhibit tetany because of the calcium-ion concentration being over 4%.

S. H. Liu, working on this subject on cases which were beginning to show the signs of osteomalacia, seems to show that in these cases exhibiting tetany the diffusible calcium is below the 4% figure.

Another point must be raised which I am unable at present to settle. Are the characteristic pain, the spasm of the adductors, the irritability of the muscles, and the tetany, of which so many of these patients complain, merely stages in a syndrome which is an essential part of the disease osteomalacia, or are they, or any one of them, a separate phenomenon? My own impression is that the spasm of the adductors, the pain and the irritability of the muscles, are all part of the disease, but as to the tetany, I am by no means sure. And whilst one is discussing the blood-calcium, one is led to ask further: If osteomalacia and rickets are one and the same disease, does the statement of Howland and Kramer about the relation of calcium and phosphorus hold good?

They say: "It would seem from a study of the calcium and phosphorus of the serum in children with rickets, and with rickets complicated by tetany, that the determining factor in the calcification of the bones is the presence of calcium and phosphorus in such amounts that the product of their concentration in milligrams per 100 c.c. of serum equals a certain minimal figure which lies roughly between 30 and 40. A study of the same elements in the serum of rats rendered rachitic by various dietary deficiencies bears out this statement. When the product is below 30, rickets is invariably present. When healing occurs as the result of any therapeutic measure, the product will be found progressively to rise."

"In the zone which may be designated the rachitic zone, i.e., below 30, are to be found cases of rickets and rickets complicated by tetany. Theoretically, it is possible to have, and actually we find in this zone, cases with high calcium and low phosphorus, cases with low calcium and high phosphorus, and cases with low calcium and low phosphorus. If either calcium or phosphorus is distinctly low, i.e., if the calcium is below 7·0 and the phosphorus below 3·5, the patient, if he be an infant, has rickets. To this general statement we have found no exceptions."

It must be noted, however, that it is clear that there are exceptions to this rule. Does this rule hold good in osteomalacia?

TABLE I.—CASES OF ACTIVE OSTEOMALACIA.

	Before Treatment				After 12 Days' Treatment			
	Calcium	Phosphorus	Product	Tetany	Calcium	Phosphorus	Product	Treatment
(1)	5·2	2·5	13·00	−	6·0	2·61	19·66	Cod-liver oil and calcium lactate
(2)	6·0	1·9	11·40	+	5·8	2·9	16·82	Calcium phosphate
(3)	7·4	1·8	13·32	+	8·7	1·0	8·7	Calcium phosphate
(4)	5·6	2·3	12·88	+	6·21	3·5	21·74	Cod-liver oil and calcium lactate
(5)	5·8	3·0	17·40	−	7·7	2·3	17·71	Calcium lactate
(6)	7·0	3·8	26·60	+	4·6	4·1	18·86	Liberal diet: milk, eggs and fresh vegetables
(7)	7·0	2·4	16·80	+	6·6	3·57	23·56	Liberal diet: milk, eggs and fresh vegetables
(8)	5·0	2·0	10·00	+	6·6	2·95	26·07	Cod-liver oil
(9)	5·4	3·2	17·28	+	7·57	1·95	14·76	Cod-liver oil

TABLE II.—ANOTHER SERIES IN WHICH TREATMENT WAS CARRIED A LITTLE FURTHER, BUT WITHOUT ANY IMPROVEMENT OF DIET.

	Calcium	Phosphorus	Product	Tetany	Calcium	Phosphorus	Product	Treatment
(1)	7·5	1·8	13·50	+	8·6	1·8	15·48	Cod-liver oil
(2)	6·4	1·2	7·6	+	8·2	2·1	17·22	Cod-liver oil and calcium lactate
(3)	6·2	2·4	14·88	+	9·5	3·0	28·50	Cod-liver oil and calcium lactate
(4)	5·8	1·6	9·2	Reflexes exaggerated	8·5	1·6	13·6	Olive oil and calcium lactate

TABLE III.—THE THREE CASES QUOTED IN THIS PAPER WHICH HAVE BEEN THOROUGHLY TREATED AND THE PATIENTS CURED OR MUCH IMPROVED.

	Calcium	Phosphorus	Product	Tetany
(1) Before treatment	10·8	3·6	38·88	–
After treatment	9·8	5·0	49·00	
(2) Before treatment	6·6	2·8	18·48	–
After treatment	8·2	4·0	32·80	
(3) Before treatment	7·5	4·0	30·00	–
After treatment	9·9	5·0	49·50	

In view of these figures it seems extremely likely that the rule which Howland and Kramer have laid down for rickets holds also in the main for osteomalacia, though it must be remembered that in adults the normal figure for phosphorus tends to run at a lower level than that of children, which would lower to a certain extent the figures for calcium and phosphorus.

It will also be noted that in the few cases which received calcium alone, there is little sign of a rise towards the normal figure, and there was little, if any, improvement in their condition. We have, so far, found it impossible, in osteomalacia, to correlate the X-ray findings with the calcium and phosphorus figures, as has been done by Weech, and it must be also noted that there is a small group of cases with marked osteomalacia in which the calcium figure appears to be practically normal.

The Ovary in Osteomalacia.—The question of the rôle, if any, which the ovary plays in osteomalacia, was raised anew by Fraser in a paper read at the meeting of the New York Obstetrical Society on March 8, 1927.

His conclusions and the descriptions of the sections of the ovary he was examining differed so widely from what we had found in Peiping, that I brought my sections home and examined them anew and compared them with those he had made. The differences were great, but may be partially explained by the fact that the ovary which he was examining was only at the fifth month of pregnancy and it is doubtful whether the appearances were not due to the exaggeration of the normal, rather than to the presence of the abnormal. We have agreed to investigate the question further. The results of therapy have, however, made it abundantly plain that even should the ovary show changes from the normal, these are consequent upon and not the cause of the disease, and castration need not be considered in the question of treatment.

What are the Earliest Symptoms of Osteomalacia?—Green-Armytage points out, and it is certainly true of the Chinese cases, that "just as rickets is a deficiency disease with multiple clinical types, so is osteomalacia," and there is no doubt that many of the earlier cases are not recognized. And in an area where osteomalacia is common, this needs to be impressed on practising physicians, for, if these early signs can be detected and treated during pregnancy, not only may deformity be avoided, but it should be possible to cure the osteomalacia in some instances before the birth of the child. And if they can be so treated, as in the case I am about to narrate, it is evidence of great value in proving the truth of our theory, that osteomalacia is a purely nutritional disease, and that the ovary plays no primary part in its production.

A Canadian woman, aged 32, was under my care during the early months of her second pregnancy, which had been risked on my specific advice. The first pregnancy had ended by a long labour with a dead child. The last monthly period was on April 2, 1928, so that her expected date of confinement was January 12, 1929. Pregnancy went on perfectly normally

till September, 1928, when she left my care to travel to her home in West China. Owing to political conditions the journey was tedious, involving almost continuous travel for six weeks, during which time she had mostly canned goods for food, was almost entirely in the shade, and took practically no exercise. On her arrival she came under the care of one of my former staff members, Dr. Gladys Cunningham, to whom I am indebted for the further history of the case.

The patient had no constipation, but was suffering from slight heartburn, for which her husband, a doctor, had been giving her calcium lactate. Urine and blood-pressure were normal, but the patient was complaining of backache, and a belt was fitted, but did not relieve the symptoms. During the latter part of October and beginning of November, 1928, the discomfort increased, and her symptoms on November 20, 1928, were as follows: Pain through the pelvic girdle, in the femora and back, sleepnessness and restlessness, a disinclination to walk with a feeling that she would break if she did so, liability to stumble, pain on flexing the thighs on the abdomen and pain in the symphysis pubis. Three days later her doctor noted that the sleeplessness was very marked, with some twitching of muscles, great restlessness, increase of difficulty in walking, with characteristic gait. The fœtus was unusually restless, flinging itself about from side to side, and kicking and humping up its back with sudden extension of the limbs. The patient had sudden unexplained attacks of nausea. Urine and blood-pressure normal. Bowels somewhat constipated. Appetite fair. Dr. Cunningham now diagnosed early osteomalacia, and the blood-calcium was estimated and found to be only 8 mgm. per 100 c.c. of serum. A skiagram of the pelvis showed rarefaction, specially marked about the symphysis pubis.

On November 24 the patient was put on full diet, with 1 grm. of calcium lactate and one and a half ounces of pure cod-liver oil daily, with as much sunlight and fresh air and exercise as could be tolerated.

By December 1 there was some improvement in walking and also in sleep, pain and restlessness, and the fœtus was not so restless.

On December 8 lightening took place, the blood-pressure and urine were normal, and symptoms were still improving.

On December 10, owing to a threatening of labour pains, patient was shaved. It was still difficult and painful to flex and externally rotate the thighs, but walking was much easier.

On December 28 patient was sleeping well, walking with comparative ease, the fœtus was not more restless than a normal one, and the blood-calcium was up to 12·4 mgm. per 100 c.c. of serum.

By January 1, 1929, patient declared that she was "at least two-thirds well." She still had a little tenderness about the hip-joints, but all other symptoms were markedly improved.

On January 9, after a dose of castor-oil and quinine, labour supervened. She could now flex and rotate her thighs with ease and without pain, and there was no trouble from this cause during delivery, which took place in normal time and without any tear. The baby was normal, weight 6 lb. 1 oz., and was reared without difficulty, the mother's lactation being normal.

That this was an early case of osteomalacia there can be no doubt. The salient points are these: Under the idea that the baby's head would be less hard, for the last two months before treatment she had taken no meat, eggs, tea or coffee. The food had been mostly canned, she had been keeping out of the sun and having little exercise. She had the typical osteomalacia gait, with the usual irritability of the adductor muscles, and the pain over back and thighs. The blood-calcium was reduced and the patient was on the verge of tetany. She reacted properly to the treatment of osteomalacia and was cured *during* her pregnancy, passed through a normal labour and did not have any recurrence of the symptoms.

Of particular interest is the observation of the restlessness of the fœtus *in utero*. Both the patient herself and Dr. Cunningham were positive that it was greatly in excess of the normal. One naturally wonders whether this was not an irritability verging on a tetany *in utero*, and I have noted this excessive movement of the fœtus in other cases, in which also it subsided under treatment. It will be noted that in this case the symptoms cleared only slowly. Much more so is this the case with patients who have suffered for some time from the malady.

Cod-liver oil and calcium lactate give excellent results, but the cod-liver oil must be given in sufficient quantity and should be pure oil and not oil-emulsion. At least an ounce to two ounces should be given daily, and I have private information of one case in which two ounces was insufficient and the addition of irradiated

ergosterol and sunlight was needed before marked improvement was obtained. Green-Armytage reports excellent results with intravenous sodium morrhuate injections and irradiated cholesterol.

There is already a good deal of evidence that irradiated ergosterol is a valuable and potent agent. Hess, Lewis and Rivkin have given details of its clinical use in cases of rickets, and, as was to be supposed, it has already proved its use in the treatment of osteomalacia. Starlinger and Hottinger have published accounts of cases showing its value, and an interesting point is that in Starlinger's case, and in one of Hottinger's cases ovariotomy had already been performed without benefit to the patient. Green-Armytage in India has proved its value, and I have had the same experience in China. Undoubtedly it is a great addition to our remedies for this disease. Hitherto I have used it in doses of 1 mgm. a day, and so far have seen nothing corresponding to Hess's cases of hypermineralization, possibly because of the low calcium figures in our cases.

We may rightly be asked whether these cures are permanent. Provided that the patient takes reasonable care, we can state positively that the cure is a lasting one. I have under present observation patients treated by me so long as seven years ago who are now quite well. Perhaps one of the best tests of the cure is the ability of the patient to pass through another pregnancy without any recurrence of the disease.

In 1924 there came to hospital a young Chinese woman, aged 21 (Hosp. No. 8206). She had come of her own volition from the north of Shansi, complaining of inability to walk, pains in the legs, and backache. Her first pregnancy had been five years previously, she had had a normal labour, and the child was alive and well. Four years ago she had a second pregnancy with a normal labour but she suffered during part of the carrying and lactation period from the pains of early osteomalacia. Two years ago she had a third pregnancy, again a normal labour, and again the symptoms of osteomalacia. Six months before admission she had ended her fourth pregnancy by a difficult labour, in which she had to be helped. She had tetany during the lactation period. Her pelvis was badly deformed and she had the typical signs and symptoms of the disease. We treated her with cod-liver oil and calcium, and she went home two months later able to walk, and having lost her pains. She continued the cod-liver oil for another month at least. In October, 1925, she returned to hospital with no signs of osteomalacia, and at full term. We delivered her by Cæsarean section of a living normal child, and she suckled the baby in the usual way. There has been no recurrence of the disease.

One has to be patient, especially in the early stages of the cure, but when improvement has really begun—and it may take a fortnight or three weeks in a severe case to do so—the cure generally progresses steadily and with a fair rapidity.

In the last paper published by Miles and myself, I described an operation devised for the relief of the disability caused by the crushing together of the ischial tuberosities and making marital relations impossible. I have now performed this operation a second time.

In the section on the deformities of the spine and chest I have given the details of Mrs. K. T. C., the third case. On April 16, 1929, this patient was put under ether, and with the assistance of Dr. Van Gorder I excised the descending ramus of the pubes, the ascending ramus of the ischium, and half the ischial tuberosity. The operation was done subperiosteally as far as possible. The patient made a rapid and complete recovery and two fingers can now be passed with ease into the vagina.

I wish to express my thanks to Dr. G. Van Gorder and other of my colleagues who have helped me by kindly transferring patients with this disease to my care; to Dr. A. A. Weech for special assistance in the consideration of the problems concerned in the relation of rickets and osteomalacia; to Dr. C. H. Hu for special help in working out the pathology of the case of antenatal rickets and the consideration of the microscopical appearances in the ovaries from cases of osteomalacia; to Dr. C. K. Hsieh for skiagrams and opinions as to their interpretation; to Dr. Bert Anderson for special work on the teeth in the case of antenatal rickets; to Dr. Curran, of Fen-chow, and Dr. Coffman, of Ping-ting-chow; and to Mr. H. S. Wang for help with the illustrations.

Section of Odontology.

[*January* 27, 1930.]

Bone-Grafting the Mandible.

By William Billington, M.S., F.R.C.S. and Harold Round, M.D.S., L.D.S.

Prior to the European war, attempts to repair gaps in the mandible by bone grafts had proved very unsuccessful and had practically been given up. The serious deformity and functional disability that resulted from wounds complicated by the destruction of large portions of the lower jaw, either at the time the wound was inflicted, or from subsequent necrosis, directed attention again to the desirability of closing the gaps by bone-grafts and invested the problem with fresh interest and importance. For three years, in association with Mr. A. H. Parrott, we were in charge of the "Jaw Centre" at the 1st Southern General Hospital, where upwards of 2,000 soldiers suffering from jaw wounds were received. A considerable proportion of these suffered from compound fractures of the lower jaw, and in many cases so much bone had been destroyed that bony union could only be secured at the expense of normal alignment and with resulting deformity, and in some the gap was so wide that any attempt to secure union by approximation was impracticable. The need for a satisfactory method of securing union by means of grafts was very great, and many attempts were made before we finally evolved a technique which could be trusted to give uniformly good results. A description of the method employed was published in the *British Medical Journal*,[1] and in the *Proceedings of the Royal Society of Medicine*.[2] In all, seventy-five cases of compound fracture of the mandible due to war wounds were successfully treated by means of bone grafts, the gap varying in extent from half an inch to five inches. The longest graft employed was seven inches in length: it was successfully used in the case of a soldier whose lower jaw, from angle to angle, had been completely destroyed.

The conditions for securing successful jaw-grafting are better in civil practice than they were in connection with war injuries. In the latter class of case we had to contend with extensive associated damage to soft tissues, and with virulent and prolonged sepsis, from which dense scars of low vitality resulted. These formed a very unsatisfactory bed into which to introduce the graft. As the result of our experience we feel justified in claiming that, provided there is no active disease present, defects in the lower jaw can be successfully remedied by bone-grafts, and firm osseous union obtained without loss of normal alignment in practically every case. The length of the gap between the fragments is immaterial. The technique is simple, but it involves close collaboration between surgeon and dental surgeon.

The mandible is peculiar in that success in grafting can rarely be obtained by the technique used in connection with the long bones. It is very intolerant of foreign bodies of any kind, and attempts to fix a free graft by wire, pegs, or plates, almost invariably led to failure. Equally, fixation by dovetailing the graft between the fragments was frequently unsuccessful. Further, fixation of the fragments by dental splints led to absorption of the graft, if carried out before the operation, or until the wound had firmly healed. After many experiments, all attempts to fix the graft or the fragments were abandoned, fixation only being secured by dental splints about three weeks after the graft was introduced and the wound firmly healed.

Pedicle grafts have a very limited application, and are only of value when the gap is a comparatively small one. A further disadvantage entailed by their use is that

[1] *Brit. Med. Journ.*, 1918, (ii), 679.

[2] *Proc. Roy. Soc. Med.*, 1919, xii, Sect. Odont., 55-72.

the fragment from which the graft is taken is weakened and greater interference with the teeth is necessary. Owing to the ease with which free grafts can be introduced, and the uniformity of success that has attended their use, the employment of pedicle grafts has been entirely discontinued.

A matter of considerable importance is the choice of the bone from which to take the graft. Rib-bone is too soft, and does not develop strength equal to that of the jaw generally. Grafts from the tibia are brittle, and cannot readily be bevelled and shaped to fit the gap; also, tibial grafts do not appear to accommodate themselves to their new environment, and are apt to necrose and work out. After experimenting with grafts taken from various parts of the body, the choice finally made was the crest of the ilium. The anterior superior spine, with the crest as far back as necessary, is freed from the attached muscles, and a graft as long as required is readily obtained by sawing through the bone below the crest from the anterior superior spine backwards. The advantages are that the graft is readily obtained and a minimum of injury inflicted—in no case has any subsequent disability been complained of. The bone is very tough and can be cut to any required shape by bone-forceps without splintering, and the graft is thick and strong. Finally, grafts obtained in this way readily accommodate themselves to their new environment, and their nutrition rarely causes any anxiety. It is quite exceptional for any indication of absorption or rarefaction to be seen on X-ray examination between the time the graft is introduced and its firm osseous union with the fragments.

Operative Technique.

Preliminary Preparation.—It is absolutely essential that there should be no sepsis present in the field of operation. If this has existed, there should be an interval of several months after all signs of inflammation have subsided and the wound has firmly healed, before a grafting operation is attempted. Unless this precaution is taken, there is a risk of latent sepsis lighting up. Great care should be taken to exclude the presence of sinuses opening into the mouth. Teeth immediately adjacent to the gap must be extracted and all septic teeth or stumps in any part of the mouth removed. Just before the operation all splints and fixation apparatus should be removed, and no splints should be introduced for at least two weeks afterwards when the wound has healed. The presence of fixation splints within the mouth causes risk from post-anæsthetic vomiting, greatly adds to the discomfort of the patient, and, where pressure is exerted by them in or near the operation area, interferes with vitality and increases the risk of sepsis.

Operation.—A curved incision is made through the skin of the neck, beginning a full inch behind the extremity of the posterior fragment and ending a similar distance in front of the extremity of the anterior fragment. The incision commences and finishes about half an inch above the line of the lower border of the jaw, and in the neck, runs about an inch below that line. This incision is deepened by cutting upwards until the lower border of each fragment is reached. The soft tissues covering the outer surface of each fragment are then raised for an inch away from the gap and turned up in the flap. The ends of the fragments, together with the intervening fibrous tissue occupying the gap, are next carefully cut away. At this stage care is necessary to avoid making an opening into the mouth, an accident which necessitates abandonment of the operation and postponement until the wound has healed. The preparation of the bed is completed by removing a flake of bone from the outer surface of each fragment for an inch away from the gap. In doing this the exposed surfaces of raw bone are bevelled a little. All bleeding is carefully arrested, and the wound covered up while the graft is being prepared.

The graft is taken from the same side of the body as the wound in the face. This ensures that the patient will be able to lie comfortably on one side when sleeping. An incision is made over the crest of the ilium, commencing at the anterior superior

spine and extending as far back as required. The muscles are then separated on either side of the crest by cutting through their attachments with a scalpel as close to the bone as possible. The soft tissues are pressed back by ribbon retractors, and the bone is made to project for nearly an inch. The graft is cut with an ordinary Horsley hand-saw with movable back. The division of bone commences in front below the anterior superior spine, and is carried back until a graft is obtained which is two inches longer than the gap in the jaw. It is advisable to measure the length required on the crest and to make a vertical saw-cut at the required spot before commencing the horizontal division. This insures that when the saw has travelled the required distance the graft becomes loose.

The detached piece of bone is held in a sterile mop, its extremities are bevelled with bone forceps, and any adhering soft tissue is trimmed away with scissors. The graft is then introduced into its bed in such a way that the bevelled ends overlap the gap by an inch at either end and lie on the prepared raw surfaces on the fragments. A little shaping is required to allow the graft to lie comfortably in place, but as the curve of the crest of the ilium approximates closely to that of the jaw, very little moulding is required. No attempt is made to secure fixation of the graft; it merely lies in the gap with its bevelled extremities extending over the fragments of jaw at either end. Two advantages result from the extensive overlapping: (1) A broad line of bony contact between the graft and the fragments is provided, with increased prospect of speedy, firm, osseous union; (2) there is practically no risk of separation in the event of the size of the gap being increased by the subsequent introduction of the dental fixation splints, as a certain amount of sliding can take place without contact being lost.

The soft tissues are sewn closely over the graft with chromicized catgut. This keeps it in place, has the additional advantage of surrounding the graft with living vascular tissue, and abolishes dead spaces in which blood-clot and serum can collect. Finally, the skin is approximated with a few interrupted stitches. No drainage is employed beyond that of leaving spaces between the skin sutures to allow of the escape of serum. A simple dressing and bandage is applied and the patient sent back to bed. The whole operation can be carried through deliberately and comfortably in about forty minutes. The patient complains of very little discomfort in the jaw, the chief complaint being directed to the wound in the hip.

No attempt is made to introduce the dental splints until the wound is firmly healed and the compound fracture has been converted into a simple one. This usually occurs in about two weeks, after which the case is treated as one of simple fracture of the jaw. Firm bony union occurs in from two to four months; but it is inadvisable to fit the final dentures until an interval of about six months from the operation.

Dental Technique after the Operation.—In from three to four weeks, according to the state of the wound and the patient, new models are taken and splints made for the fixation of the jaw in correct alignment. Any slight alteration in the occlusion, or any displacement of the fragments, which may have resulted from the operation or in the interval prior to the re-adaptation of splints, is found to be easily reducible. This is possible owing to the fact that the graft, whilst being firmly held in position by the deep layer of soft tissues, overlaps the fragments at each end, and a certain amount of sliding can take place without bony contact being lost. The correction and retention of the fragments in their required positions is attained by the use of articulating splints—silver cap-splints adapted and cemented to any standing teeth, such splints being supplemented by vulcanite extensions. These extensions are lined with soft rubber where covering edentulous parts in the neighbourhood of the graft, in order that the parts may be retained in position with a minimum amount of pressure. The splints are fixed to each other by means of articulating tubes and bolts. In many cases it is possible to retain or refix the original splints used to

preserve alignment pending the operation. In such cases it is only necessary to bolt these together after the lapse of the usual period following the operation.

Cases.

To-night we have shown three cases of bone-grafting the mandible, two of them being quite recent, but they are all three of special interest.

(1) A boy, aged 8, who, at the age of $6\frac{1}{2}$ years, had a portion of the left side of the body of the mandible removed on account of sarcoma. A little more than six months afterwards a bone-graft was inserted with successful result. This, we think, constitutes the youngest case of bone-grafting the mandible on record (fig. 1).

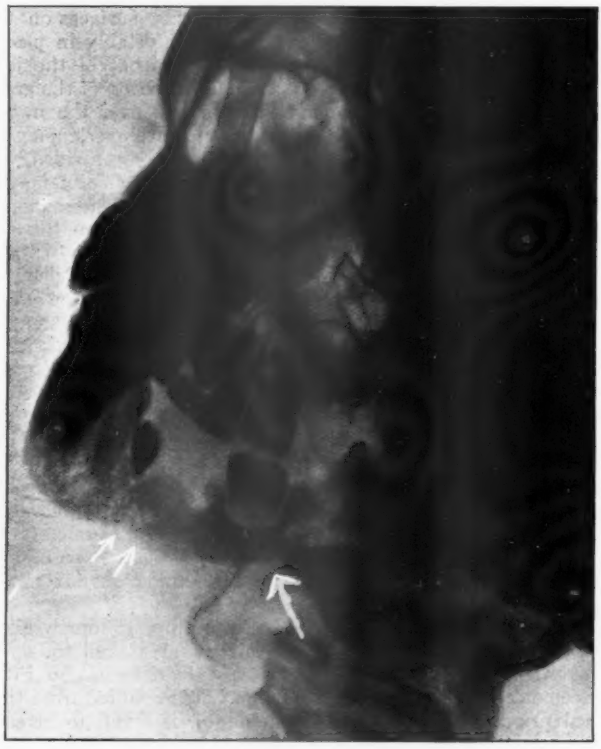


Fig. 1.—Case 1. Present state of graft.

(2) A man, aged 51, who, at the age of 11, had a portion of the mandible removed in the region of the left canine to the first molar, presumably on account of sarcoma; for forty years he carried on with two floating fragments until a bone-graft was inserted last May, with successful result. This, we think, constitutes the oldest case on record (figs. 2 and 3).

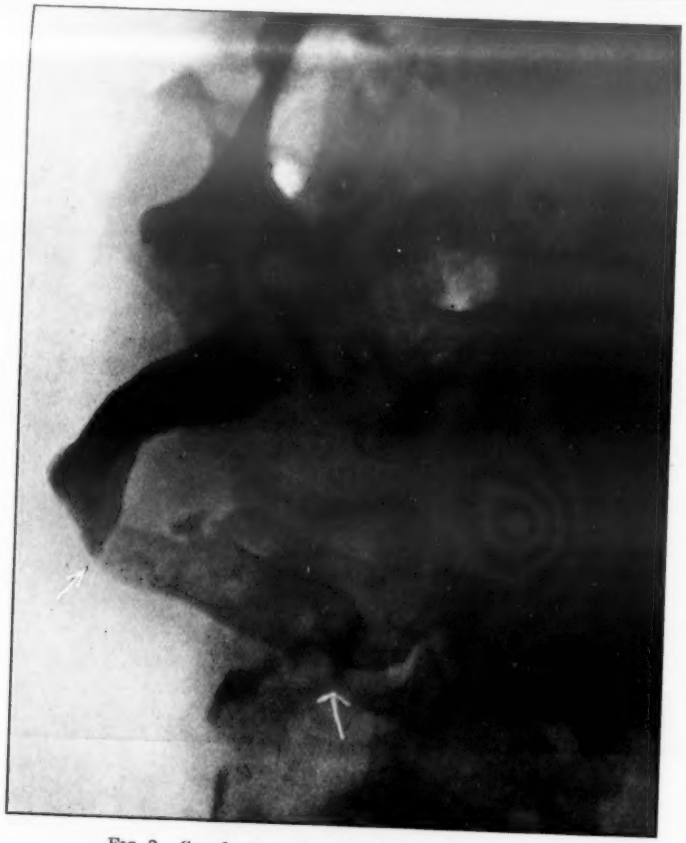


FIG. 2.—Case 2. Present state of graft. Lateral view.

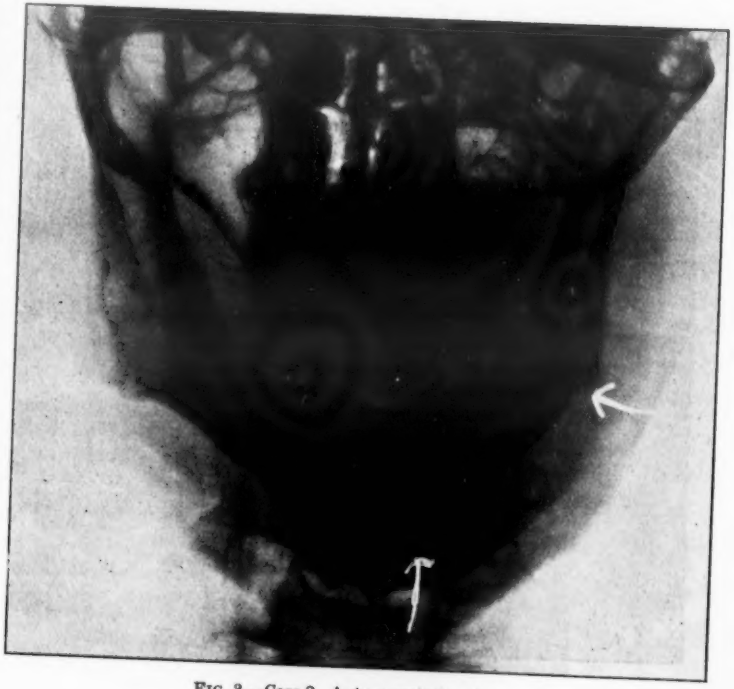


FIG. 3.—Case 2. Antero-posterior view.

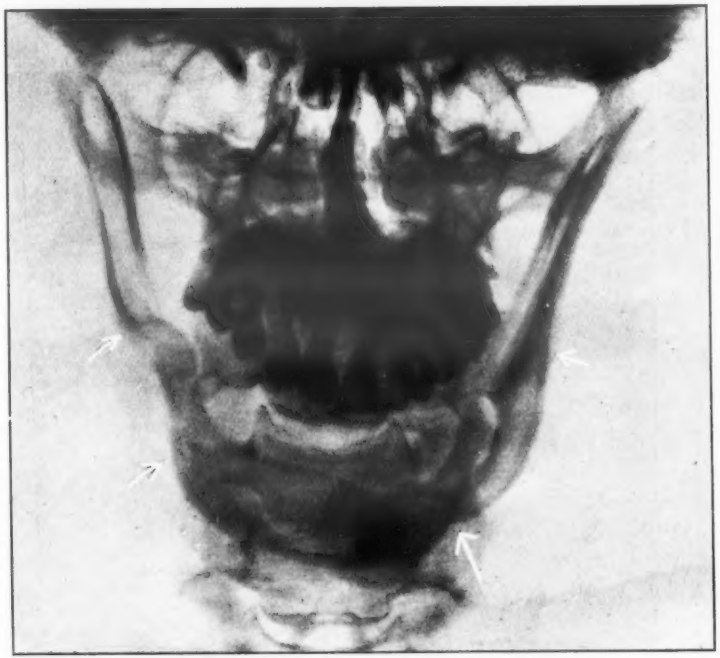


FIG. 4.—Case 3. Present state of grafts. Antero-posterior view.

FIG. 5.—Case 3. Left side.

FIG. 6.—Case 3. Right side.

(3) A man, aged 33, who has a bone-graft on each side of the body of the mandible, the left side to bridge a gap caused by war injury, the right side to bridge a gap caused by necrosis, following a fracture resulting from a blow (figs. 4, 5 and 6).

Since the war the various civilian cases in which we have bone-grafted the mandible number about twenty; the ages of the patients varying from 6½ years to 51 years, and the cases include those in which gaps have been caused through gunshot injuries, removal of growths, necrosis, osteomyelitis, odontomes, etc., and in all of them success has resulted and union at both ends has been obtained without any further interference.

A Two-stage Operation for Cleft Palate.

By WILLIAM BILLINGTON, M.S., F.R.C.S., and HAROLD ROUND, M.D.S., L.D.S.

LANGENBECK'S operation for cleft palate, in spite of the fact that it cannot be successfully carried out until the child is about three years old, is still the one most generally employed. Alternative procedures, the chief attraction of which is that they are possible during the first few weeks of life, have not proved satisfactory, and to a large extent have been abandoned in this country. It has been

found that the greater defects in speech that follow postponement of the closure of the cleft can very largely be remedied by competent instruction. A successful result by Langenbeck's method gives a thick satisfactory palate, with comparatively little scarring, but the soft palate is tighter and less mobile than normal. It does not appreciably interfere with the normal development of the maxillæ or with dentition. A defect that often persists is inability to approximate the soft palate to the posterior wall of the pharynx, and so to separate completely the oral from the nasal airway. This interferes with perfect phonation, although the impairment can be largely overcome by education. An ingenious supplementary operation upon the posterior wall of the pharynx has been devised by Mr. E. M. Wardill, of Newcastle, to remedy this defect by making the pharyngeal wall project forward and so fill the gap. In other words, the pharyngeal wall is made to approximate to the palate instead of the palate to the back of the pharynx.

We have very carefully considered the contention of H. D. Gillies and W. Kelsey Fry that early closure of the hard palate causes appreciable contraction of the maxillary arch because of the pull of the scar tissue resulting from the operation. We rather think that the main factor is a developmental one, and due to the failure of bony contact at the anterior alveolar margin, that is, to the failure of one or both maxillary processes to fuse with the premaxilla. This condition exists in all cases of complete cleft and is responsible for asymmetry of growth on the two sides, with consequent faulty articulation of teeth. It is a noticeable fact that distortion of the arch and faulty articulation are much more marked when the cleft has been complete, whether closed early or left open until adult age, than when there is fusion of the maxillary processes with the premaxilla and the cleft in the hard palate is incomplete. Where the cleft is complete it seems desirable to introduce bone into the gap in the alveolus at as early an age as possible. This might be achieved by utilizing a displaced premaxilla or by a small bone graft. We cannot too strongly support Gillies and Fry in their contention that closure of the soft palate as early as possible is of great value in subsequent treatment, but cannot agree that it is an advantage to leave the hard palate permanently open.

Though generally successful when performed at the usual age for clefts of moderate width and extent, Langenbeck's operation often fails when the cleft is unusually wide and extends through the alveolus. It is often extremely difficult to obtain satisfactory results in older children and in adults, when no previous attempt at closure has been made, or when an attempt has been made and has failed.

Two conditions are essential if successful results are to be obtained. (1) The flaps must be freed sufficiently to allow of approximation in the middle line without lateral tension, otherwise the stitches will tear through. (2) The vitality of the flaps must be adequate to ensure healing.

It is very difficult—and often impossible—to secure both these conditions at one operation. When the cleft is wide and long, the necessary trauma and interference with blood-supply is so great that the vitality of the flaps is reduced until they can barely maintain their own life, and are unable to effect healing between the pared inner edges, no matter how carefully they are sutured together.

It is a frequent and disappointing experience to find that healing has failed wholly or in part, even though everything appeared quite satisfactory when the patient left the table. It is a curious fact that throughout the extensive literature of cleft-palate surgery, little attention has hitherto been paid to the importance of adequate nutrition of the flaps at the time they are sutured together. In the Jaw Centre of the First Southern General Hospital during the late war we found that it was frequently necessary in plastic work upon the face, after raising pedicle flaps of skin for the purpose of repairing defects, to postpone suturing them in position until there had been time for recovery from trauma and diminished blood-supply. Acting upon the experience so gained, it occurred to us that the successful closure of

clefts of the palate might be better secured if the operation were performed in two stages instead of one. In this way it is possible to obtain the two required conditions for success when it is impossible to do so at one sitting.

The ordinary Langenbeck technique has been followed, with such modifications as are required in individual cases. In the first operation the flaps are raised and reflected inwards, separation being carried out sufficiently freely to allow of their easy approximation. As maintenance of vitality is of less importance than when

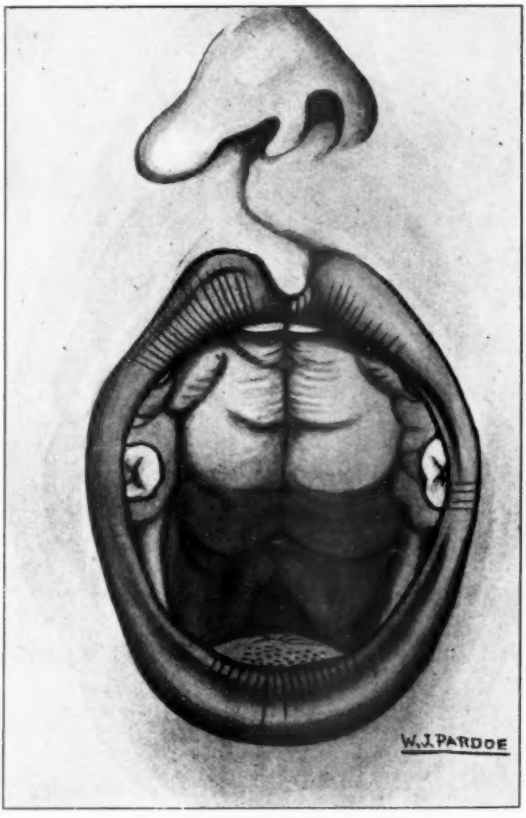


FIG. 1.—C. F., aged 6¼. Complete right lateral cleft and hare-lip. Lips closed at 7 months. No attempt to close palate until 6 years old when it was completely closed by two-stage operation. Occlusion poor; contracted arch.

the operation is completed at one sitting, the separation of the flaps can be carried out more freely, and freedom from all lateral tension secured. The lateral grooves are then lightly packed with gauze and the patient sent back to bed. The gauze is removed after twenty-four hours, and it is not re-inserted, as its presence seems to cause irritation and keep up sepsis. In ten days' time the second stage of the operation is carried out. With a few light touches of an elevator the flaps can be pushed together. The inner edges are then pared and the sutures inserted. Fine

silkworm gut has proved the most suitable suture material. This stage of the operation is greatly facilitated by the absence of the free bleeding which generally follows the initial incisions required for the raising of the flaps, and which may seriously obscure the field of operation. In the second operation the anterior part of the cleft, when it extends through the alveolus, can be closed by a small flap taken from the lip. The sutures are removed on the twelfth day.

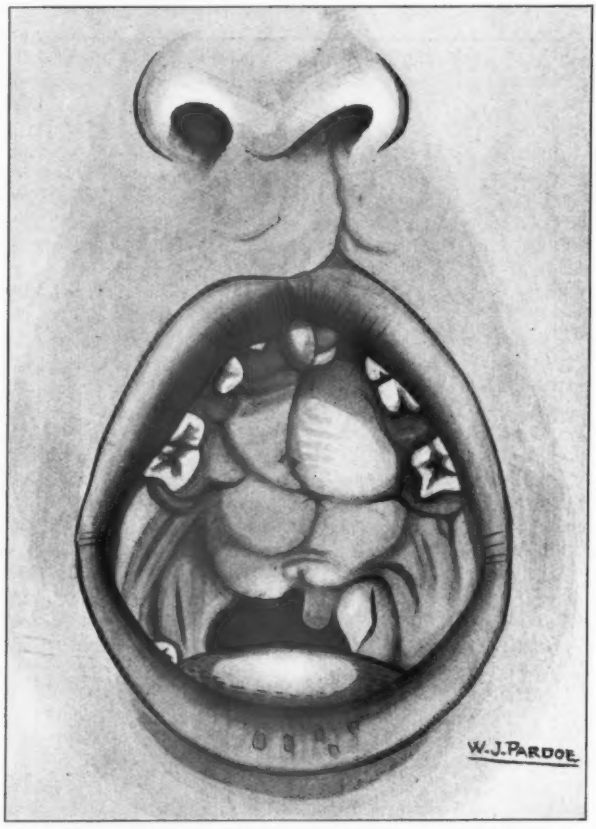


FIG. 2.—H. B., aged 11. Complete left lateral cleft and hare-lip. Lips closed at 18 months. Palate attempted at 2½—failure. Nothing further done until 9 years old, when cleft was successfully closed by two-stage operation. Occlusion poor; contracted arch.

This two-stage operation has given almost uniformly successful results and has enabled us to treat adult cases of cleft-palate which had been regarded as hopeless. In some of these it has been necessary to make the soft palate almost entirely from the lateral walls of the pharynx. In one case, that of a girl of 23, in whom earlier attempts by other surgeons had completely failed, there was no trace of a soft palate and the hard palate was represented by a strip of mucous membrane, about

three-quarters of an inch wide, on one side only. The failure of the earlier operations had resulted in sloughing of the entire flap on the left side and of the posterior half of the right one. A soft palate was made of flaps reflected from the lateral walls of the pharynx, and subsequently the gap in the hard palate was filled by a pedicle flap composed of the mucous membrane lining the sulcus on the outer side of the alveolus and the cheek, and this was introduced through a space created by the extraction of the second and third molar teeth. The result was very good, a

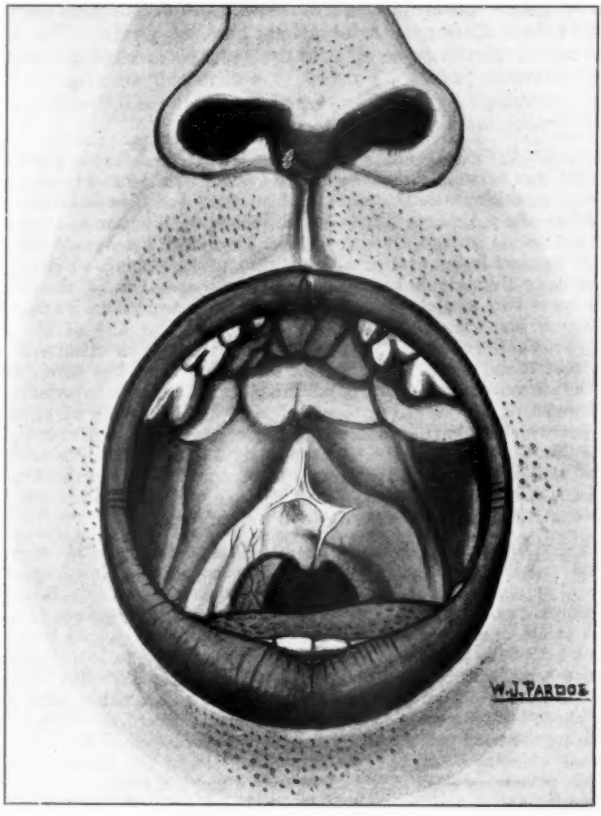


FIG. 3.—H. C., aged 22. Complete bilateral cleft with double hare-lip. Attempt to close palate when lip was closed at 3 months, palatal attempt a failure. Cleft completely closed by two-stage operation eight years ago, when patient was 14. Occlusion bad; contracted arch, poor development of maxillæ.

small opening in the anterior part of the hard palate, close to the line of the teeth, being the only defect. In these cases in which new tissue has had to be introduced to obtain a satisfactory result surprisingly little inconvenience has been caused by the scars in the pharyngeal walls and no complaint has been made.

We have had no experience of the two-stage operation in babies under three years old, but the results in older children and in adults have been so gratifying that it seems worth while attempting it at a much earlier age than is possible when the

whole operation is carried out at one sitting, If thought desirable, the soft palate only might be closed and the closure of the hard palate postponed to a later date.

In view of the fact that so much greater certainty of a successful result is given by the two-stage operation it is questionable whether it ought not to be the routine procedure in all cases. The shock and risk generally are diminished by it, as the length of time required for each stage is less than for the whole operation and the child has time to recover from the effects of the first operation before the second is carried out.

A very striking and gratifying result of the closure of the cleft in late cases has been the psychological improvement that has followed. The retiring self-consciousness and "inferiority complex" that was so marked a feature previously has almost entirely disappeared. Further, it is surprising to what an extent speech defects can be minimized by the efforts of an intelligent adult patient assisted by an expert in voice production.

Discussion.[1]—Mr. P. P. COLE said that Members would recollect a stand-up fight in the early stages of the war between those who wished to obtain union at any price and those who declared that such a position was untenable. The victory had been in favour of bone-grafts. His own operation—the pedicle operation—which Professor Billington had decried, had proved in his (Mr. Cole's) hands universally successful. In civil life it was applicable to 90% of cases and could be used in connection with gaps up to 4 cm. long. Evidently the pedicle operation in Professor Billington's hands and the pedicle operation in the hands of himself and his pupils were two entirely different things, and it would be interesting to know if Professor Billington had seen either himself (the speaker) or any of his pupils perform the operation. Professor Billington had said that the rib was an unsuitable bone for such cases, alleging that it did not afford sufficient strength. That was surely contrary to the mechanics of bone development in the body. Professor Billington's experience in connection with the intolerance of the jaw to foreign bodies of any kind was at variance with that of other workers who had carried out any considerable amount of bone-grafting of the mandible. He (Mr. Cole) failed to see how the interval of two or three weeks would prevent absorption or weakening of the graft alleged to be produced by the presence of splints at the time of operation. Professor Billington's own method was simple, and, for that reason, it should rank as one of the procedures available to the surgeon.

Mr. W. KELSEY FRY submitted a number of slides to illustrate his views on methods of fixation, and stressed the necessity, in certain cases, of holding fragments in splints to the correct alignment before bone-grafting was done. Professor Billington had said that trauma resulted from the use of splints, but he (the speaker) had not found it so. With regard to cleft palate operations, he (Mr. Fry) regretted that surgeons were again concentrating on closure of the hard palate. Dental surgeons were able to do that more satisfactorily with a vulcanite plate, and for that reason Mr. Fry advocated closure of the soft palate rather than of the hard. If surgeons were able to close a hard palate after they had closed the soft one, without bringing the soft palate a millimetre forward, he would be glad to see the result. By closing the hard palate at the expense of the soft palate, the speech would suffer. If the hard palate was closed and the soft palate half-closed, the dental surgeon was called upon to close the remaining part, which was a very difficult matter.

Mr. T. POMFRET KILNER said that during his six years' experience of bone-grafting at the Queen's Hospital at Sidcup, and later at Roehampton, it had been unusual for a week to pass without at least one mandibular bone-grafting operation being performed, and during his last three or four years there, about two-thirds of these cases passed through his hands. The authors of the paper had rightly emphasized the need for close coöperation between dental and operating surgeons, a point which could not be too strongly stressed. He felt that one of the most valuable things was missed if splints were not employed at the time of operation. The main object of a bone-graft in this region was so to place any remaining lower teeth that they might function in proper occlusion with their fellows in the upper jaw. Splints fixed before operation indicated with precision the gap which must be filled in order to ensure this result. He could see no reason why such splints should affect the graft adversely, or produce irritation and increased risk of infection. He

[1] The two papers were discussed together.

particularly stressed the necessity for freeing the posterior fragment, even to the extent of resecting the coronoid process, in order that the reconstructed jaw should have its condyles in similar position. He could not see how this was to be achieved with an edentulous posterior fragment without some form of fixation of the graft. When teeth were available for the purpose, his patients were invariably splinted for operation. Grafts were always wired in position by wire mattress sutures which, even in edentulous cases in which splinting was impossible, provided most efficient immobilization. He had habitually used an area of bone different from that described by Professor Billington and Mr. Round, namely, a half-thickness slice from the outer surface of the ilium, including half the breadth of the crest. This produced even less disturbance than when the whole crest was removed. The graft was always dovetailed to correspond with the raw surfaces of the fragments obtained by freshening them at the expense of their outer surfaces. He had no statistics to offer, but he thought that 4% or 5% would be an outside estimate of trouble from infection in a large and completely unselected series of cases. He showed slides prepared from radiograms of three cases to illustrate the extensive overlapping of graft and freshened fragments, the mattress wires in position and the correction of malposition of the edentulous posterior fragment. He also showed slides of two other cases of extensive reconstruction of the whole chin region, in which very long curved bone-grafts had been employed.

On the subject of cleft palate he would offer only a word of criticism. The incisions represented in the diagrams described by Professor Billington appeared to be much nearer the mid-line than those employed by most surgeons and the muco-periosteal flaps were therefore much narrower than usual, and must be robbed of a considerable proportion of their blood supply. He suggested that this might be the reason why it had been found expedient to adopt the two-stage method of repair.

Mr. ARTHUR H. PARROTT said that some speakers appeared to think that deformity of the fractured jaw, previous to the bone-grafting operation described by Professor Billington, had not been corrected in any way. Having worked in conjunction with Professor Billington during the late war on these cases and having seen the uniformly successful result of the simplified operation described, he was able to assert that this was a mistake. Mr. Round in his paper had specifically mentioned that "splints were removed from the mouth immediately prior to the bone-graft operation." These were splints which had been adapted to a final corrected alignment of the fragments as achieved after all sepsis, scarring, etc., had been dealt with. The interval elapsing without splints, while the graft-wound was healing by primary union, produced little relapse or contraction at that period and it was generally quite feasible to replace the same splints without alteration when that primary healing was complete, the shape and size of the graft allowing sufficient movement for this. A striking advantage of Professor Billington's method was the abolition of the necessity for insertion of foreign bodies such as wires, screws, or plates, with their added risk of sepsis and absorption.

Mr. G. G. EXNER said that it seemed now to be generally recognized that the hip bone constituted the best source of bone-grafts. Splinting immediately after the operation, however, gave better results than splinting after a three weeks' interval. He thought that the incisions for the operation were too low in the neck and that an æsthetic effect seemed to have been left out of consideration. Regarding the cleft palate operations: it was Wolff who first recommended that all cleft palate operations should be carried out in two or three stages and his results seemed to justify his theory. In the cases shown this evening, it seemed to have been the main object to close the palate, irrespective of the phonetic result, which could not be considered satisfactory. The operation of Professor Billington for obtaining the flaps in two stages was certainly good, but in cases in which there had been no previous operation and in which no cicatricial tissue was present, this was unnecessary, as the blood supply was adequate. In cases that had already been operated upon, possibly more than once, the method now generally adopted and recommended by Pichler, Ernst, and others, was to do the operation in two stages: (1) closure of the hard palate only, without any incision into the soft palate; (2) operation on the soft palate.

Professor BILLINGTON (in reply) said that Mr. Parrott had already dealt with the subject of splints, which were prepared before the operation and re-inserted afterwards. It was found that patients were more comfortable and the results better when splints were removed before the operation and left out for a reasonable time afterwards. The discovery was made quite accidentally in the case of a soldier of turbulent character who had taken

out his splints and thrown them away. It came as a matter of some surprise to find that his was the first really satisfactory case. The procedure was then adopted generally with uniformly good results. He (Professor Billington) did not desire to decry the pedicle graft. He himself had hesitated to employ it because of the amount of disturbance involved in obtaining a satisfactory result. The method he had dealt with in his paper had been employed successfully in just under a hundred cases. Twenty-five civil cases since the war had been so treated with uniform success. Other methods in other men's hands might give equally good results. With regard to foreign bodies, he had not found that the jaw was tolerant of wires and splints. Moreover, they were not necessary.

He agreed with Mr. Fry, for whose writings he had a great respect, that it was most desirable to secure a soft palate at the earliest possible moment. All the patients seen that evening were late cases, and most of them had arrived at an age when development of the bones had practically ceased. With one or two exceptions the soft palate had been non-existent, and the problem had been to attempt to create something of a soft palate. He had been assured by dental surgeons in the Midlands that they preferred to handle a patient with a closed hard palate rather than one with the hard palate widely open. In cases in which a soft palate could only be made from the walls of the pharynx, criticism that it was impaired if the hard palate was closed, disappeared. Professor Billington added that during the war he had, though an abdominal surgeon, been placed in charge of a large jaw department through which 2,000 men had passed. His interest in that branch of surgery had been maintained and he still received a considerable number of civilian cases and continued to employ the technique that he had found so satisfactory during the war.

Section of Urology.

[*January* 23, 1930.]

Pathology and Treatment of Carcinoma of the Penis.

By A. Clifford Morson, F.R.C.S.

Abstract.—There are two types of penile cancer, ulcerative and papilliferous, the predisposing causes of which differ. In the second variety a wart initiates the malignant changes, whereas in the former, phimosis and decomposition of smegma are the predominant factors.—The clinical manifestations of carcinoma of the penis are profoundly different from those of glandular carcinoma.

Treatment may be either by amputation (Gould operation) or radium irradiation.—A cure is certain if the growth is removed by complete amputation, but though the results from irradiation are variable, it is the treatment of choice, on account of the moral effect of rapid disappearance of the tumour with retention of the organ.—Direct treatment of the glands in the groin is not advised unless the skin over them is involved.

If research into the literature is a true guide to progress in medicine, a sorry tale has to be told in respect of advancement in our knowledge of the pathology of penile cancer during the past fifty years. The clinician on the other hand can claim that sixteen years ago he introduced a remedy which has superseded with some success the mutilating operation of total amputation of the penis. This remedy, of course, was the exposure of the growth to radium irradiation.

When it is remembered that the last paper of importance by a British surgeon on the subject of carcinoma of the penis was written in 1882, it is opportune that the present position of the pathologist and the clinician in relation to cancer of this organ should be once more carefully reviewed.

Fifty years ago it was known that malignant disease of the penis commonly occurred in those with a long prepuce, that it was of slow growth, that it readily became septic, and that enlarged glands occurred in one or both groins. Treatment had consisted in partial amputation.

Taking each item seriatim, let us compare our knowledge of to-day with that of 1880. Firstly, what are the factors which lead to the production of carcinoma of the penis? Is it only the long prepuce which predisposes to this disease? The sweeping statement has been made in most books on the subject published during half a century, that carcinoma cannot arise in those who have been circumcised. In most cases this is true, but I have performed partial amputation for a growth of the glans penis where no prepuce existed (fig. 1). Dr. Ray, of Calcutta, states that he has observed two cases in Mohammedans who had been circumcised between the ages of 5 and 10.

It has been suggested that the prolonged pressure of the prepuce gives rise to circulatory disturbances in the glans. The changes induced are known as hyperplasia, leucokeratosis and leucoplakia (fig. 2). Moreover, the retention of smegma sets up inflammatory processes which must certainly predispose to cancer formation.

A. L. Dean, of New York, has made a clinical study of seventy-five cases between the ages of 21 and 79. There were no Jews in this series, and 60% of the patients gave no history of venereal disease. The latter statement brings us no nearer to the determination of predisposing causes unless amplified by a description of the variety of cancer met with in each case. A wart on the penis is not considered by the layman as venereal in origin, and when seeking advice for the treatment of these tumours he usually denies having contracted the disease. Such warts are the

result of sexual intercourse and most certainly are the forerunners of the papillary type of penile carcinoma. In fact, here is one more example of an innocent new growth becoming malignant. Warts of the penis are commonly multiple and so is the papillary carcinoma, hence the terms "implantation growth," "kiss cancer" and "contact cancer." A very good example of this may be seen in figure 3, which shows a growth arising from the region of the frænum and in contact with the main malignant mass on the glans penis. The tumour has probably been formed as a result of an abrasion of the inner surface of the prepuce and subsequent implantation

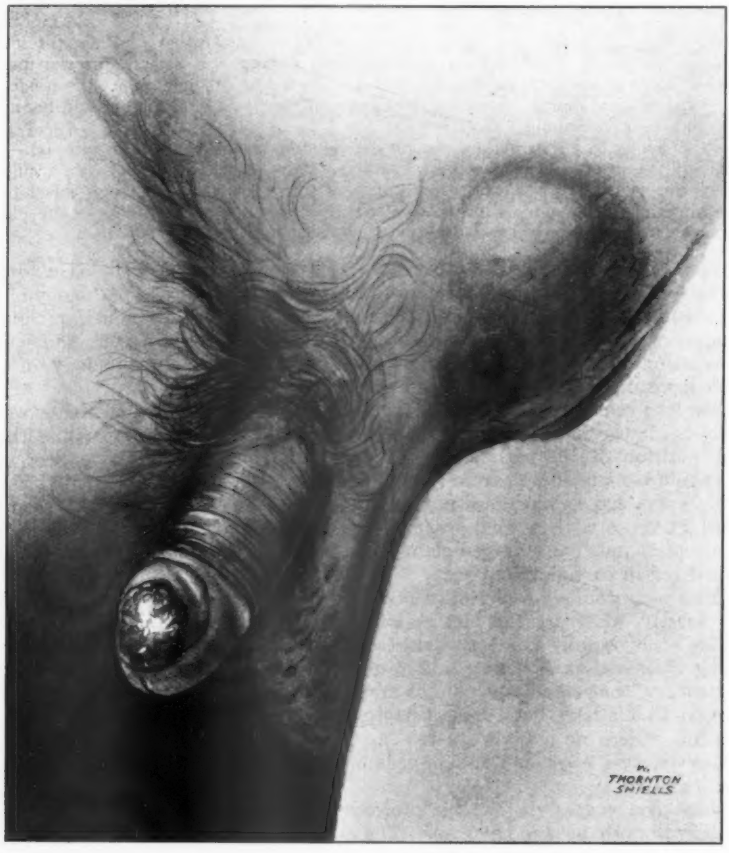


FIG. 1.—Carcinoma of the glans penis in a patient, aged 73, who had been circumcised in youth.

of cells derived from the original lesion. This mode of spread of malignant disease is a curse to surgeons, for the deposit of even one cell on healthy tissues surrounding an operation area, suffices to nullify the effects of excision of the primary growth.

From a consideration of the possible causes of papillary carcinoma, it is natural to turn to the second type met with on the penis, namely the ulcerative variety. Here we have a form of the disease which is marked by destructive habits. There is no tumour, in the sense of an outgrowth of tissue, but there is an ulcer, which, if

untreated, will eat away the whole organ. What are the causes of this deadly phenomenon? Does venereal disease play a part? There is no evidence of it. On the other hand, I am unaware of any such case in which decomposition of smegma and phimosis have not been present. They are the predominant factors in association with the formation of the malignant ulcer.

Here we may summarize our knowledge of the influences which are at work in the production of penile cancer. There are two types: (1) The papillary which is preceded by the appearance of venereal warts and in which phimosis does not necessarily play a part. (2) The ulcerative, the predisposing causes of which are phimosis and decomposition of smegma.

The causal agent of both remains a mystery, but dirt plays a most important part in both varieties. Those who have practised personal hygiene are immune from this disease.

A characteristic of penile cancer is its chronicity. The presence of a swelling has been known to a patient not for months, but for years. In one case the growth had

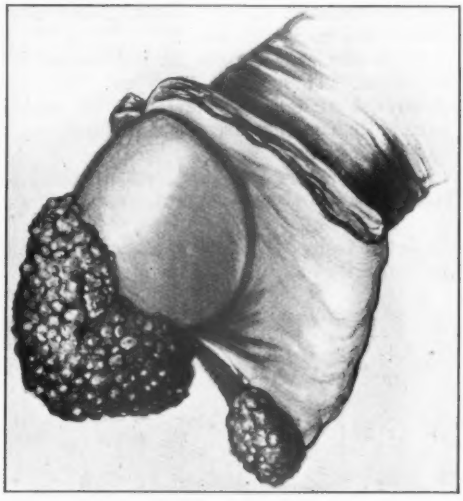
FIG. 2.—Penis showing a patch of leucoplakia on the glans and also around the frænum.

been discovered nine years previous to submission to radical treatment. The reluctance of both men and women to seek medical advice on immediate discovery of a painless lump is still far too common. So far as penile cancer is concerned, there is no excuse for such negligence, when it is borne in mind that no other part of the body is seen and handled more frequently.

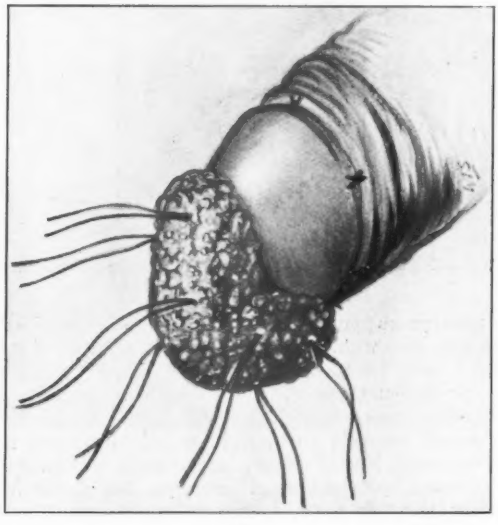
The onset of sepsis compels an appeal for help from the medical profession. Until then there is no pain, loss of weight, or cachexia, and only the smallest degree of discomfort. With the introduction of infection, the glands in the groin become enlarged and tender; there is fever, and wasting commences. The tumour itself becomes active, and makes war on the surrounding tissues.

The involvement of the lymphatic glands is a matter of considerable importance from the standpoint of treatment. An inquiry into this aspect of the disease is necessary for a full understanding of the differences which exist between it and glandular carcinoma. In my experience, the migration of the malignant cell from the primary lesion to the glands of the groin is delayed until the cancer has passed the

initial stage and become infected. The increase in the size of the glands is due to adenitis and not to malignant metastases. This observation brings one to a study of



A)



(*B*)

FIG. 3.—Papillary carcinoma.—(*A*) The prepuce has been slit to show a contact growth in the region of the frænum. (*B*) Shows the method of insertion of the radium needles.

the final picture, which immediately precedes death. Those who have had the opportunity of watching these cases from the beginning to the end will retain a last-

ing impression of the virulence of sepsis in the presence of cancer. It is the former, not the latter, which is the actual cause of death. I have seen cavities in both groins large enough to hold a tangerine orange, filled with the most offensive discharge. The final scene is alarming, even to those accustomed to witness severe hæmorrhages. For some days there will be an ominous oozing of blood, and

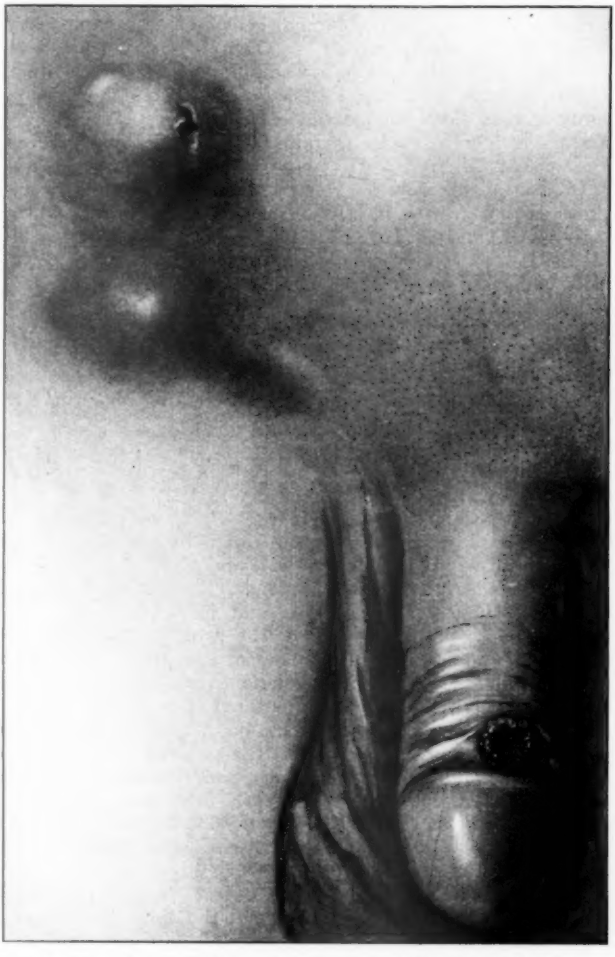


FIG. 4.—Malignant melanoma of the penis in a man aged 77. Note that the glands in the right groin are full of the pigment melanin.

then quite suddenly the common femoral artery ruptures. The unfortunate patient is almost drowned in his own blood within a few minutes.

Post-mortem Findings.—The disease is terminated by secondary hæmorrhage, due to ulceration of the femoral vessels. A search for metastases other than those already known to exist in the inguinal glands gives a negative result. The solid

organs show those changes which are the direct effect of septicæmia. Sometimes instead of hæmorrhage, septic broncho-pneumonia is the terminal condition.

This absence of distant deposits is common to carcinomata of the skin, as for example, rodent ulcer, tongue, and lip cancers. Why does the squamous cell fail to get past the glands in the immediate neighbourhood of the parent growth? Can there be some peculiar local resistance in this type of cell in the gland filter, which is absent in the case of spheroidal and columnar cells? Or in squamous-cell carcinoma are we confronted with a disease which is called "cancer" from want of greater knowledge? The clinical manifestations are so different from those of spheroidal-cell and columnar-cell growths that suspicion arises as to whether after all the term "cancer" is only used to cloak our ignorance.

I pass on to consider in detail certain facts in relation to the incidence of carcinoma of the penis. Firstly, it will be agreed that in this country the disease is rare. During the past eighteen years I have not seen more than twenty-five cases. At Whipps Cross Hospital, with its 400 male beds, the average is little more than 2 per annum. At St. Mary's Hospital, Islington, with 300 male beds, 1·5 per annum, and at St. Peter's Hospital 2 per annum, yet A. L. Dean, of New York, has made a clinical study of 75 cases.

Walther states that penile cancer is three times more prevalent in negroes than in whites. This observation is confirmed by certain French writers, but no explanation is offered.

The period of life when the disease most commonly appears is between the fourth and sixth decades. Pfadder and Widmann record a case in a boy aged 18 on whom they performed amputation.

Some difference of opinion exists with regard to the percentage of patients with glandular enlargement, C. P. Howse stating that in his series the inguinal glands were involved either by infection or carcinoma in 94%. In my experience this estimate is too high, 60% being nearer the mark. Barringer's opinion, with which I entirely agree, is that the invasion of the groin glands by carcinoma is rare, and that infection without cancerous involvement is quite common.

Directly sepsis invades the inguinal glands, the patient's general condition steadily deteriorates. Fever is continuous and cachexia becomes a prominent feature of the illness. As previously stated, the primary lesion has begun to eat away the whole organ, and in place of a single orifice, there are multiple openings through which the urine trickles. In my experience retention never occurs.

Before a description of the treatment is entered upon, mention must be made of the malignant melanoma or melanotic carcinoma, which occasionally attacks the penis. The clinical course in this situation is the same as that in any other part of the body; a pigmented mole or wart of many years' standing is followed, without obvious warning, by rapid dissemination and early fatal termination. I recorded a case of this kind of which less than ten appear in the literature, in the *Proceedings* of this Section two years ago (fig. 4). The patient, aged 77, was admitted to the Whipps Cross Hospital for retention of urine due to an enlarged prostate. The pigmented mole on the skin of the dorsum of the penis was disregarded until enlarged glands appeared in the right groin, about the time the urinary obstruction occurred. The primary growth together with the skin of the dorsum and the glands in both groins were removed in one mass. The retention of urine was treated by suprapubic drainage. It will be noted that the glands in the right groin were full of melanin. (See fig. 4. Sometimes the pigment appears in the urine.) The patient survived the operation nine months, when he died with multiple metastases. Permission for a post-mortem examination, unfortunately, could not be obtained. In connection with pigmentation of the skin of the penis, Shattock has stated that in uncircumcised negroes the skin of the glans is the same colour as the white man's, but, after removal of the prepuce, becomes black, the scar on the other hand remaining white.

The clinician must, of necessity, make a careful study of pathology, but his chief concern will always be to acquire a profound knowledge of treatment. It will, therefore, be of interest to trace the attempts made during the last fifty years to cure penile cancer. Before 1882, treatment, apart from the use of cauterizing agents, consisted in rapid removal with the amputation knife of the whole or part of the penis. Enlarged glands in the groins, as a rule, were left alone. In 1882 the late Sir Alfred Pearce Gould described a technique which consisted not merely of amputation of the whole of the penis, but removal of the crura, the bulbo-cavernosus muscle and the glands in both groins, the cut end of the membranous urethra being stitched to the skin of the perineum. Some surgeons of more recent date have advocated the operation which used to be practised on prisoners of war by the Abyssinians, in whose temples can still be seen bas-reliefs of the results of total extirpation of the external genitalia. The next step forward took place in Paris in 1912 and 1913, when tubes containing radium were buried in the growth. Since then various modifications of this line of treatment have been tried, and to-day a concentrated effort is being made to banish the knife and replace it by the radium needle.

In performing partial amputation it is important to make a posterior or ventral flap to prevent the urine from trickling over the wound. Also a considerable length of urethra should be dissected out distal to the point of division of the corpora cavernosa, to allow for retraction. The stitching of the cut end of the urethra to the buttonhole in the skin-flap must be so arranged as to cause eversion of the mucous membrane of the new external meatus. This technique assists in preventing subsequent narrowing of the lumen. The only advantage of this operation is that it preserves a portion of the penis and is attended with a minimum of shock. It can only be performed for a growth confined to the glans penis. Now that radium has come into its own, the disadvantages of partial amputation are obvious to all. There are, therefore, left in competition the Gould operation and radium irradiation.

Little need be said concerning the technique of total amputation, for it is well known and practised by every surgeon of experience. The insertion of the urethra into the skin of the perineum is a simple matter, but to prevent contraction of the new external meatus is far from simple. I know of no technique which will avoid this defect. The prognosis is just as satisfactory as is excision for early rodent ulcer. The main disadvantage of this operation is the loss of the organ. If the operation is properly performed there is never any recurrence of malignant disease. The term "cure" can be used with every justification provided that at the time of operation infection is limited to adenitis.

W. M., aged 66.—April, 1923: Large growth of the penis—urine passes through several openings along course of urethra. Glands in both groins hard and nodular. Fever present. Gould operation of complete amputation. January, 1930: No glands palpable in groins. Bougie 15F passed once a fortnight. General health excellent.

We now pass on to a consideration of the technique of radium irradiation.

So controversial is the question of dosage, that no satisfaction will be gained by joining issue with any one school of thought. The important point is that there is no known law governing the sensibility of cells to irradiation, or to put it in another way—two similar tumours arising in two individuals of the same age, treated under exactly the same environment, and with the same dosage, will not produce exactly the same response to irradiation.

There are two methods of applying radium to a growth of the penis. Some surgeons place a Columbia paste cap, in which are inserted the radium containers, over the whole growth and leave it in position for from one to ten days.

My own practice up to date has been to use platinum needles, 0·5 mm. thick,

with overall length of 22·5 mm. each containing 5 mgm. of the element, and to bury them in the growth about two centimetres apart, so as to produce homogeneous irradiation of the whole tumour. For the initial exposure each needle has been left in position for twenty-four hours, for every subsequent one, thirty-six hours. This increase in the time of exposure is necessary on account of the greater resistance of the malignant cell to irradiation if its nucleus is not destroyed at the commencement of the treatment. Every effort is made to give a knock-out blow to the whole tumour at the initial irradiation, but some of the cells may escape, especially those in the vicinity of the parts of the needles which contain no radium. In 1914 I performed an experiment to demonstrate this point.[1] In order to protect the skin of the scrotum and the testicles from the rays, a lead plate must be placed between these structures and the penis. The plate should be sufficiently long to allow each end to rest on the thigh. For the introduction of the needles, local anæsthesia suffices, such as freezing with ethyl chloride, or, if circumcision is needed, infiltration of the tissues with 2% novocain.

The changes in the tumour which can be observed with the naked eye, commence about the third day after irradiation. In the papillary variety, the projecting parts of the growth become smoothed out, and a thin whitish film due to keratinization appears over the whole surface. If a lethal dose has been given the tumour will have disappeared in a fortnight. When a malignant ulcer is treated, the base is replaced by healthy granulation tissue in the course of from ten to twenty-one days, and normal squamous epithelium commences to grow in from the edges. The complications of treatment by radiation are difficulty in micturition—caused by œdema of the urethral mucous membrane, sloughing—the result of overdosage—and stricture of the external meatus.

A study of the literature shows how diverse are the views with regard to the treatment of the inguinal lymphatic glands. Regand says that the glands should be treated before the initial lesion, presumably by the external application of radium. Proust and Maucer, of the Belgian School, hold the opposite opinion. Barringer advocates leaving the adenitis alone, as he believes that infection is eliminated by its control at the source, i.e., the penis. I, personally, neither operate upon nor irradiate the inguinal glands unless the skin over them has ulcerated, my reasons being as follows: If the squamous cells of a penile cancer have entered the inguinal glands, they will go no further. If the primary growth has been eradicated, these cells will not multiply but will be ringed round by a defensive mechanism in the form of fibrosis, which will ultimately ensure their sterility. When enlargement of the glands occurs, the increase in size is due, in the large majority of cases, to adenitis, which can be controlled and even eliminated by removal of the penile growth. I am fully aware that in holding these views I may be accused of heresy, but at least I have the consolation of knowing that the treatment outlined has been to the advantage of my patients.

The danger of dissecting out the lymphatic tissue is twofold. Firstly, lymphatic œdema may result, comparable to the condition known as "brawny arm" following the radical operation for carcinoma of the breast; and secondly, there may be an extensive cellulitis, due to operative interference in tissues heavily charged with infection. If my views on lymphatic invasion are accepted, such treatment after irradiation is merely meddlesome.

Finally, we reach the all-important question: When is the primary growth to be irradiated, and when is it to be removed by operation? Surgeons are probably unanimous in their view of the value of the Gould operation in eradicating the disease. The functional result, so far as micturition is concerned, is also satisfactory. There is complete control. Narrowing of the external meatus frequently occurs,

[1] *Proceedings*, 1914, vii (Sect. Path.), 97-108.

and requires intermittent dilatation with bougies. This defect and the loss of the whole organ are the two great disadvantages of this method of treatment.

On the other hand, by irradiation, the penis is preserved and though stricture of the external meatus may sometimes result, its frequency is not comparable to that observed after amputation. As experience has taught us that cancer of this organ can be cured by amputation, strong evidence in favour of irradiation treatment must be brought forward if it is to replace the knife.

I have had under close observation for the past twelve months, four cases of carcinoma of the penis, three of the papillary type and one ulcerative, all of which have been treated with radium.

(I) W. J., aged 57.—Gonorrhœa 30 years ago. Small wart on glans penis. January, 1929: Tight prepuce. Cauliflower growth of glans penis. Urine being passed at right angles to penis. No fever. One small gland in right groin and a number of enlarged glands in left groin.

January, 1929: Five tubes of 5 mgm. each and one tube of 25 mgm. inserted into circumference of growth for 24 and 12 hours respectively. Fluorescein 2% painted on growth. In 24 hours no visible change. Second day marked loss of vascularity—passing urine freely and direction approaching normal. Third day, more marked loss of vascularity. Fourth day, growth shrinking—some œdema of skin. Sixth day growth rapidly shrinking—patches of leucoplakia at right side of insertion of needles. Urinary meatus now clear of growth.

April, 1929: Two tubes of 5 mgm. each inserted into growth for 17 hours. The exposure ought to have been for 36 hours, the tubes being removed in 17 hours in error.

November, 1929: Nodule size of small pea. Two tubes of 5 mgm. each for 36 hours.

January, 1930: No glands in groins. Slight surface slough on dorsum of glans penis. Micturition normal. Has put on 10 lb. in weight since January, 1929.

(II) A. E. D., aged 41.—Nine years ago treated for wart on the penis at the Lock Hospital.

April, 1929: Now has a cauliflower growth the size of a tangerine orange surrounding the whole of the glans penis. Offensive discharge. High fever, cachexia, enlarged glands both groins. Urine passed in several small streams through growth.

Six tubes of 5 mgm. each inserted into growth at two centimetres from one another for 24 hours. At the end of this time the position of the tubes was changed, and they were reapplied for another 24 hours in a new site, and so on, for five days, until the whole tumour had been irradiated.

Growth shrank in size and at the end of April no longer fever, and glands hardly palpable.

May, 1929: One needle of 5 mgm. inserted for 24 hours into piece of growth.

November, 1929: Three needles of 5 mgm. inserted into lateral recurrence for 36 hours.

Present condition: In excellent health. One gland palpable in left groin. The glans penis is almost entirely destroyed by the growth except for a portion which is attached to the penis by a thin pedicle. Much deformity of tissues around the terminal end of urethra. No difficulty in micurition.

(III) I. W., aged 70.—Phimosis since birth.

May, 1929: Cauliflower growth of glans penis with contact growth on prepuce. Enlarged glands both groins. Urethral opening obscured by growth.

Circumcision performed and growth on prepuce removed.

Seven needles of 5 mgm. each inserted into growth on glans penis and retained there for 24 hours. Fluorescin 2% painted on growth.

January, 1930: No enlarged glands in groins. No signs of growth. Skin near frænum rather sore owing to rubbing of clothes on a surface which has always been covered by the prepuce.

(IV) G. F., aged 62.—Denies venereal disease. Ulcer on penis for six years.

July, 1929: Carcinomatous ulcer surrounding corona of glans penis. Fever, cachexia. Palpable glands in both groins. Patient very dirty.

Six tubes of 5 mgm. each inserted into ulcer and retained for 24 hours on dorsum. Owing to summer holidays patient not seen for two months.

September, 1929: Six tubes of 5 mgm. each for 36 hours, placed laterally.

January, 1930: Patient very dirty. Palpable glands in left groin. Growth on dorsal aspect disappeared; still growth on either side of frænum.

Conclusions.—In either the papilliferous or the ulcerative variety, the growth can be made to disappear, but there is no guarantee that the patient will be cured. The general state of health rapidly improves. Enlarged glands in the groins shrink and many disappear. The moral effect of removal of the tumour, with retention of the penis, makes irradiation the treatment of choice. As penile cancer is a surface growth, recurrence can be readily treated by further irradiation. If this fails, at all events the patient's health will be so much improved that radical cure by the Gould operation can be effected with a minimum of surgical risk. If the disease is so far advanced that the greater part of the penis has been destroyed, the correct treatment is total amputation. It is possible that with a sufficient quantity of radium the growth can be made to disappear, but the consequent deformity and functional result will be deplorable. Finally, the only indication for direct treatment of enlarged glands is when the skin over them is ulcerated. They should then be dissected out.

Discussion.—Mr. FRANK JEANS (President) said he had not himself treated many cases of carcinoma of the penis with radium, but he agreed that the psychological effect of retaining the penis to the patient was important, and had a beneficial effect on his health. There was much to support the idea that epithelial carcinoma was checked by the glands in the groin, and he hoped it was true. He remembered a case of carcinoma of the colon, operated upon by Paul, by his own (Paul's) method. The operator felt glands in the mesentery, and did not attempt to restore that colotomy. Many years afterwards the patient asked to have the colotomy closed. Paul had thought the condition must be carcinoma. He closed the colotomy and searched for glands, but did not find any, therefore the enlargements previously felt must have been inflammatory. The enlargement of glands in the case of epithelioma of the penis was also largely inflammatory; he would like to feel that it was entirely so.

Mr. F. FOWLER WARD said that he had cases in which the Gould operation had been performed nine or ten years previously, and there had been no recurrence. One of his patients had died from what might be called a secondary effect in the lungs. The only immediate fatality among these cases was one in which he (the speaker) had torn the femoral vein, and the patient had died from embolism within half an hour. All the others had done well. In five of the ten cases the patients were still alive and well. In two recent cases he had left the corpora cavernosa, doing a Young operation. He had had a third case, in which a man had been circumcised. Possibly he had had venereal disease. The condition was supposed to be a small papilloma on what remained of the prepuce, and when that was removed it was found to be carcinomatous. The patient had done well up to the time of his death in an accident.

Mr. FRANK KIDD [communicated later]: Mr. Morson gave the impression that in his opinion, cancer of the penis should be treated as a local disease which seldom caused secondary deposits in the lymphatic glands or other parts of the body. This was a revolutionary idea that could not pass unchallenged. Surgeons were aware that in the early stages of septic cancer on mucous membranes or skin, the regional glands were usually enlarged as a result of chronic infection, and that if the primary septic growth were removed the glands might rapidly subside. But this fact did not in any way alter the well-established surgical principle that no treatment of a cancer was adequate unless it included excision of the regional lymphatic nodes whenever practicable, or at the very least some method of treatment of these nodes by radiation. Even though in some cases the regional nodes were not cancerous but septic, this fact did not absolve us from the duty of excising them. Only by so doing could we make sure of excising those glands that were affected by cancer. Mr. Morson by his own confession had made no attempt to treat the regional glands in the three cases shown treated locally by radium. His action transgressed a first surgical principle, and could not be allowed to pass without comment. The extraordinary thing about this was that in another part of his paper he had given a harrowing description of deaths from hæmorrhage from the femoral artery caused by ulcerating malignant glands of the groin secondary to carcinoma of the penis. Mr. Morson seemed to imply that the literature on the subject was silent or worthless from 1880 till the present time, and that no progress had been made during that time in knowledge of the pathology and treatment of the disease except in the discovery of the therapeutic results of radium. Such a view was an exaggeration. For instance, there

was an outstanding paper by Barney, of Boston,[1] well known as a careful and reliable worker. He analysed 100 cases of carcinoma of the penis, ninety of which he traced to a final result. Venereal disease and phimosis were the only definite predisposing causes. The warty type was of slow growth and less malignant than the ulcerating type. The disease either ran a very rapid or a very slow course; there were few intermediate cases. The regional glands were enlarged in seventy-five cases, *and were proved to be cancerous in sixty cases.* The deep pelvic glands became early involved when the disease had invaded the corpora cavernosa. Numerous distant metastases occurred in the spermatic cord, rectum, prostate and vesicles. Abdominal, thoracic and other far-distant metastases occurred in nine of the cases. Forty-two per cent. were cured by operation which included excision of the regional glands. After operation there were twenty-one recurrences in the stump of the penis, and only five in the glands of the groin. Barney's series contained no Jews and no negroes. He (the speaker) had seen a case in a negro. The cells of the growth did not contain any pigment, in striking contrast to the pigmented cells of the normal skin in their neighbourhood.

He wished to protest emphatically against the present-day fashion of some of those who were working with radium, to exhibit their cases so early after treatment. None of Mr. Morson's cases had been treated for longer than nine months. Were we to understand that these cases had been brought forward as cured by radium? He (Mr. Kidd) doubted if any one of them was cured in the true sense of the word. We were all familiar with the remarkable fact that the application of radium could destroy a localized collection of cancer cells. This was a very different proposition from curing the whole deep extent and spread of a cancer. He would put a five years' limit at least before trying to evaluate the position of radium in bringing about a cure. As a result of his own experience he was going back more and more to the use of the knife for cases that held out a hope of cure, and was more inclined to reserve radium as a palliative treatment in inoperable cases.

Mr. Morson would have us believe that by using radium to destroy the local growth in cancer of the penis we were thereby enabled to preserve the penis as a useful organ. Of the three patients shown by Mr. Morson one had certainly had his penis ruined by radium, and the other two were not so very presentable.

Some years ago he (Mr. Kidd) had shown to this Section five cases of cancer of the penis treated by complete amputation with excision of the testicles and regional glands. Good reasons could be advanced for removing the testicles when carrying out complete amputation. In the first place the scrotum, if left behind, was apt to impede micturition and to become liable to a urinary dermatitis. There was also a good psychological reason for removing the testicles. It was far kinder to the patient to do so when removing the penis. The internal secretion of the testicle drove the patient's mind to lustful desires. If these patients were castrated they ceased to be worried by these desires and their minds were able to adapt themselves peaceably to the changed condition. If the testicles were left behind such psychological adaptation was rendered difficult. The adaptation needed on the part of the wife was a more difficult problem, but he did not feel that the wives of the patients shown by Mr. Morson would have any more reason to be satisfied than would the wives of the patients he had castrated. In carrying out the complete operation he had not experienced any undue difficulty with sepsis, and he had had no trouble with stricture of the urethra, as after removal of the testicles it was possible to leave a projection of the corpus spongiosum of the urethra and graft it with a skin flap. This step seemed to prevent stricture.

Mr. R. H. JOCELYN SWAN said it would be agreed that enlargement of the glands in cases of carcinoma of the penis was nearly always due to septic infection rather than to secondary glandular cancerous metastasis, though, no doubt, secondary glandular metastases did occur in the inguinal glands. In criticism, however, he would say that the infection did occasionally go further than the inguinal glands and was not limited at this area, as Mr. Morson seems to suggest, and he could produce evidence of that. He had himself had a case of advanced carcinoma of the penis in which not only were the inguinal glands enlarged, but there was a tumour in the right iliac fossa, and the patient had died from hæmorrhage into the bowel. A large mass of glands was found post mortem in the iliac fossa; these had ulcerated into the iliac artery, which in turn had ruptured into the cæcum, and caused the fatal hæmorrhage. And that was not an isolated case.

All who had to deal with many cases of cancer would realize that the prognosis in the papilliferous type was always much better than in the ulcerative, whatever the site of the cancer.

[1] Barney, J. D., *Ann. of Surg.*, 1907, clxxx, 890.

As to radium treatment, none could yet say they had a cure in a case, because a sufficient time had not elapsed since this treatment was started; but he would like to speak on one or two points in the technique. Each surgeon had his own ideas as to dosage; he, personally, would rather employ somewhat small doses of radium over a long time than large doses for a short time; in other words, he preferred 1-mgm. needles to 5-mgm. needles. He thought it much better not to insert the needles into the growth, but rather to use a barrage of radium round the growing edge of the cancer; more satisfactory results were obtained in this way.

It would be agreed that of all forms of malignant disease, the epithelial type—as seen on penis, tongue, lip and cheek, and anal canal—was particularly benefited by radium treatment. This type was much more favourable for that treatment than the glandular type of growth, and penile carcinoma came into the category of squamous carcinoma.

He had at present several cases very like those Mr. Morson had described, but he was afraid they were not cured. In some he had had to remove the infected inguinal glands. In other forms of squamous carcinoma, the primary growth could be, as it were, melted away and quickly disappeared with radium, but radium and X-rays were not so effective in the treatment of the glands. The more he saw of radium treatment in these cases, the more he was convinced that one might treat the primary growth successfully with radium, but that glands must be removed by block dissection.

Mr. Morson had mentioned as one of the sequelæ of removal of glands in the groin, a massive œdema of the leg. He (Mr. Swan) had a case in which a Gould operation had previously been performed and nine months ago the patient had come to him with massive œdema of both legs. He thought there were diffuse recurrences of the cancer in the groins, but the swellings were now subsiding, and the patient was showing very considerable improvement.

Mr. H. W. S. WRIGHT said that in China he had treated many cases of carcinoma of the penis, which appeared to be a common disease in that country. In the absence of reliable statistics it was impossible to say just how common it is, but some idea might be gained by the fact that among ten or fifteen urological beds there was nearly always one case. Phimosis, venereal disease and dirt, pedunculated and sessile papillomata, all were also very common, and it was difficult to avoid the conclusion that the sequence was of material significance in the ætiology of the disease: although in a particular case it was impossible to assess the importance of any one factor. In most of the cases the growths were of the cauliflower type, all of them were far advanced, and in some the penis was completely eaten away.

Pathological examination had revealed nothing new. Sections were cut at half-inch intervals right down to the crura, and it was rare to find any trace of growth more than an inch away from the visible border. In nearly all the cases there were enlarged glands but only from 5-7% of these contained secondary deposits. Carcinoma of the penis was therefore in the majority of cases, including even the advanced ones, a local disease, and for this reason it seemed a pity that a controversy as to operative versus radium treatment should develop. Any treatment which dealt with the local condition was likely to be successful, and we should employ that treatment most suitable to the case under consideration.

As no radium had been available for his use in China, he and his colleagues performed something approximating to a Gould operation, and in many of the cases the size of the growth made this the method of choice. He made a gland dissection previously, because if this was not done then, it was never done. It was extremely hard to explain to a Chinese peasant, who came to hospital on account of a large lump on the penis, the significance of a small one in the groin. Some sepsis nearly always followed the gland dissection, but this did not interfere with the amputation, which was done about ten days later.

He could not see the logic of Mr. Morson's position in not removing the glands. Granted that these were involved in only a small percentage of cases, to any one who had seen a patient die from secondary hæmorrhage from the femoral artery, there was sufficient reason for removing this possibility at the cost of a small operation.

At one time he had had a good deal of trouble with stricture, and since most of the patients lived at a distance it was essential to prevent this. He had found that if about half-an-inch of cavernous tissue were left out of the wound, and no attempt was made to dissect out, or cut flaps from, the urethra, there was practically never any stricture.

He had lost one case from general septicæmia, and had seen another in which there were secondary deposits in the pelvis, in spite of a radical amputation and a gland dissection, but was unable to say to which type the primary growth belonged.

Mr. MORSON, in reply, said that the discussion had emphasized—more clearly perhaps than he could have done in his paper—certain points of great importance in the treatment of carcinoma of the penis.

He had thoroughly enjoyed Mr. Kidd's remarks, but Mr. Kidd was under an entire misapprehension in thinking that he (Mr. Morson) advocated radium treatment as a certain cure.

With regard to metastases in relation to carcinoma of the penis, he would give an instance of a surgeon who described a case of a growth of the penis with priapism. The patient had died, and post mortem, metastases were found in many parts of the body. Though clinically there had been no evidence of malignant disease of the prostate, the post-mortem examination revealed its presence. He (the speaker) had studied malignant disease of the prostate probably more closely than he had studied carcinoma of the penis, and he had seen cases of so-called penile cancer, in which the primary lesion was in the prostate. In those cases in which metastases had been found elsewhere than in the inguinal glands, the primary lesion was in the prostate and not in the penis.

In Mr. Swan's case in which there was a mass in the right iliac fossa, this swelling must have been due to an extension of the inguinal adenitis and infection of the surrounding tissues.

With regard to the loss of the diseased organ Mr. Kidd seemed to be extremely lucky in having patients who were contented with the absence of the penis. He regretted to say that in the case of the only man he (the speaker) had shown to-night who had no penis his home had been broken up in consequence of the operation, and he had a sad story to tell concerning his home conditions.

War Section.

[*February* 10, 1930.]

Cardiac Functional Efficiency in the Young Male Adult.

By H. A. Treadgold (Wing-Commander, R.A.F.).

At the present time, eleven years after the conclusion of the European war, there are 16,000 ex-Service men receiving pensions on account of so-called functional heart disease, and this fact appears to me ample justification for laying stress on the importance of a careful scrutiny of the cardiovascular system as a whole, prior to entry to the Service. The problem is not merely the elimination of organic heart disease but the equally important decision as to whether the heart is likely to withstand the acute physical and mental stress inseparable from modern war, and it is the purpose of this paper to discuss some of the means at our disposal to secure this end.

In the first place, I propose to deal with certain points of value in routine clinical examination, then to deal with the differential diagnosis of doubtful valve-lesion heart cases, and lastly to discuss how far it is possible, by simple and rapid methods, to estimate the degree of cardiovascular stability an individual possesses, i.e., his likelihood of withstanding physical or mental stress without his cardiovascular system, as a whole, showing objective or subjective deterioration.

Clinical Examination. (*a*) Inspection.—A minute or two spent on careful examination of the chest in a good light is never wasted. Pulsation of the vessels of the neck, the presence or absence of thyroid enlargement, the general musculature of the shoulder, back and abdomen, spinal curvatures, if any, and malformations of the chest itself, particularly in the heart region, should be noted, as well as the character and position of the apex-beat, and the presence or absence of epigastric pulsation—in a normal well-developed young adult it should be absent. The inner aspect of both arms should be scrutinized for visible pulsation of the brachial arteries, bearing in mind in this connection that arteriosclerosis can occur with comparative frequency in the young adult and not solely in middle age or later.

(*b*) Palpation.—The palm of the hand should invariably be used for palpation of the heart as a whole, to determine the presence of thrills, if any, and the character of the apex-beat prior to its more exact localization by the forefinger, bearing in mind that this is the point lowest down and farthest out which definitely lifts the finger. If in doubt as to whether it is in the fifth or sixth space, find the ridge on the sternum formed by junction of the manubrium and gladiolus. The second space is immediately below this. An apex-beat in the sixth space is no evidence *per se* that the heart is enlarged.

If epigastric pulsation is present and palpable, it may be due to two fundamentally different causes, viz., cardiac or aortic. If due to transmitted aortic pulsation, it can be felt along the length of the abdominal aorta, and if timed with the apex-beat, is found to be delayed. Suprasternal pulsation is also a common accompaniment of the condition, which is generally of neurotic origin and usually associated with cardiovascular instability.

If epigastric pulsation appears to be of cardiac origin, a good method is to stand behind the patient and place the fingers of the left hand over the upper part of the left costal margin. If the heart can be felt beating downwards and inwards against the fingers, it is suggestive of right ventricular enlargement.

Examination of the brachial arteries gives a far better idea of whether thickening is present or not, than does examination of the radials. Not only can a larger portion of the circumference be felt, but the fingers can be run up and down the vessel to determine whether thickening, if present, is uniform or irregular. It is as well to ask the patient whether he is right- or left-handed, as early arteriosclerosis may be found only in the right arm in a right-sided individual and vice versa. Volume and tension should be noted at the same time.

(*c*) Percussion.—May be of value as regards determining the size of the heart in a thin individual, but it is, at best, an unreliable and misleading sign in well-covered or emphysematous patients. An apex-beat definitely seen and felt internal to the nipple line in the fifth space, in an otherwise normal chest, is far stronger evidence of the probable absence of cardiac enlargement than a problematical dullness to the right border of the sternum is of its presence. When the apex-beat can be neither seen nor felt, recourse to the X-rays becomes essential before enlargement can be definitely negatived. The orthodiagraph is of the greatest value for accurate work in this connection. In this apparatus the X-ray tube is freely movable in any direction parallel to the screen. The one in use at the Central Medical Establishment has a single lever controlling the tube movements and diaphragm. After a quick look at the chest as a whole, the aperture is cut down to 1-2 square inches, and the outline of the heart and chest marked with a glass pencil on the screen, and a permanent record is then made on to translucent paper. By this means the very considerable distortion caused by the nearness of the tube to the chest is avoided, and once the technique is mastered, the margin of error is within 5 mm.

The size and height of the aortic arch, as well as the size of both auricles and ventricles, can be quickly and accurately determined by placing the patient in the right and left oblique positions. The apparatus is not at all costly, and is of great value in the accurate estimation of the cardiac area. This can be estimated from the drawn outline of the heart by the planimeter, or more simply by taking the maximum transverse diameter of the heart, which should be less than half that of the chest.

The variation in size and shape of clinically normal hearts is considerable, and as a general rule, individuals with a history of heavy physical work or continued athletics have larger hearts relative to the chest size than those of sedentary workers. This, after all, is only to be expected if the myocardium shares in the general increased musculature in these individuals. There is no direct evidence that physical stress alone is capable of causing damage to a healthy myocardium. [Here orthodiagraphs were shown illustrating various types of normal heart.]

(*d*) Auscultation.—In any case of doubt the heart should be listened to with the patient standing, after exercise, and in the left lateral position.

(1) Arrhythmias.—The stethoscope is the best means of studying alterations in rhythm, as by this means beats are detected which might not otherwise be noticed at the wrist. Sinus arrhythmia is usually of no significance, and nearly always disappears on exercise, but if extremely marked, the rate can actually double with respiration, and such cases are nearly always associated with other signs of cardio-vascular instability. Extrasystoles are evidence of irritability in the myocardium, and may be auricular, ectopic auricular, nodal, or right and left ventricular. They occur most frequently in the left lateral position, and their diagnosis is usually easy by the compensatory pause that follows them, but occasionally numerous extrasystoles may be almost indistinguishable from auricular fibrillation. Not long

ago I saw a case in which various doctors had made notes of marked irregularity for over ten years. It had been variously described as "sinus arrhythmia," "extrasystoles," or merely "irregular heart," but, on electrocardiographic examination, the heart was found to be fibrillating. The officer in question had played sixteen sets of tennis the day before I saw him, had no cardiac enlargement and was in perfect health. Right ventricular extrasystoles are possibly the commoner form met with in the young adult, and are probably extracardiac in origin, e.g., from pressure from a dilated stomach. They are relatively more frequent after a meal than before it. Auricular and nodal extrasystoles are often found associated with over-smoking. When extrasystoles disappear on exercise, as they usually do, they can be safely disregarded in an otherwise normal heart, but if exercise increases them they should be regarded with suspicion, especially if they are auricular, as this variety is a common percursor of auricular fibrillation. There is only one method of satisfactorily diagnosing a doubtful arrhythmia, and that is by the electrocardiogram, and the following records show various types of extrasystoles, both appearing and disappearing on exertion. [Here electrocardiographs of various types of extrasystoles at rest and developing under physical stress were shown on the epidiascope.]

(2) Heart Sounds.—Reduplicated heart sounds are extremely common in the young adult. A reduplicated first sound can be distinguished at the apex in well over 50% of young adult hearts. The terms "blurred," "impure" or "prefixed" first sounds are often applied to this condition. This variety of reduplication usually goes in the left lateral position. A reduplicated second sound is not so common in the standing posture but can frequently be heard in the left lateral position after exercise. A triple rhythm is also of comparatively frequent occurrence at the apex in this posture, without necessarily having any clinical significance *per se*. Widening of reduplicated sounds after exercise, especially when associated, as is frequently the case, with a poor quality first sound, a tic-tac rhythm, an increased pulmonary second sound or a triple rhythm at the apex, is suggestive of myocardial mischief. This condition frequently occurs after acute infections such as diphtheria, tonsillitis and influenza, and can, I think, be reasonably regarded as evidence that the myocardium has shared in the general toxæmia. The pulse is not necessarily raised and the condition is often missed on that account. In the absence of severe cardiac stress, it is rare for the heart to receive permanent damage, and recovery of myocardial tone is usually a matter of a few weeks, but I feel sure that many cases of gross myocardial damage discoverable in later life, date from some acute infection, followed too soon by severe physical stress.

(3) Murmurs.—One of the most difficult problems we have to face is the differential diagnosis of a reduplicated first sound at the apex, and the presystolic murmur of a suspected mitral stenosis. A reduplicated first sound can produce a very good imitation thrill at the apex, especially when the first element is soft and the second short and sharp, and on auscultation it can be equally deceiving. Points of value in distinguishing the two conditions are:—

(*A*) In favour of reduplication: (1) the absence of a rheumatic history; (2) a normal-sized heart; (3) absence of an accentuated pulmonary second sound; (4) reduplicated first is heard best over a large area of the heart and often clearest at the tricuspid area; (5) it is apt to disappear in the left lateral position or at any rate alter in spacing; (6) a big pulse-pressure.

(*B*) In favour of mitral stenosis: (1) rheumatic history; (2) evidence of cardiac enlargement; (3) the presystolic murmur increases on exercise and in left lateral position; (4) second pulmonary sound usually accentuated; (5) the murmur is accentuated after exercise and the left lateral position and is usually localized just internal to the apex-beat; (6) the pulse-pressure is always small; (7) pulse volume is small.

A closely reduplicated second sound whose second element is softer than the first can also closely simulate a short aortic diastolic murmur, and if associated, as it quite easily can be, with a big pulse-pressure, a collapsing pulse, and capillary pulsation, all of which may be present, in the absence of an aortic lesion, it may often present equal difficulties in diagnosis. Although a high pulse-pressure of 80 or over is usually present in aortic regurgitation, the systolic is rarely over 140, and a blood-pressure of 170/90 is nearly as much evidence against it as a blood-pressure of 130/50 is in favour of it. A difference of up to 20 mm. between the leg and arm systolic pressures may be found normally, the leg being the higher of the two, but a leg pressure of 40 mm. or more higher than the arm is strongly in favour of aortic regurgitation.

There is little doubt that in the past undue importance has often been attached to apical systolic murmurs and there must be a large number of perfectly normal individuals who have been diagnosed as having valvular disease of the heart, whereas in practice there is nothing whatever the matter with it. Apical systolic murmurs after exercise in the left lateral position can be detected in at least half the normal young adult hearts examined ; in the absence of other corroborative signs of mitral regurgitation they have probably no pathological significance. In the young adult there is to all practical purposes only one cause of acquired valvular disease, namely rheumatic infection of the heart, and if this could be safely excluded, the assumption that organic valvular disease was absent could be safely made in the great majority of cases. Unfortunately, not only can rheumatic infection occur apart from the joints, but the heart can be the sole site of the lesion. The fact remains that we should be chary of diagnosing organic mitral regurgitation in the absence of the supporting evidence. Slight relative mitral incompetence undoubtedly occurs, after other acute infections than rheumatism, due to the stretching of the mitral orifice as a part of the general myocardial atonia, but it has a strong tendency to disappear as the system as a whole throws off the effect of the toxæmia and returns to normality.

I do not wish to imply that a loud systolic murmur partially or actually replacing the first sound, constant in all positions, and conducted out to the axilla, can be disregarded. It cannot ; but a soft apical systolic murmur accompanying the first sound and varying with position or respiration, in an otherwise normal heart, is of slight, if any, significance. Other systolic murmurs, apart from those of congenital heart disease, are too numerous to specify in detail, but two in particular are worth noting in the young adult : the aortic systolic so often accompanying hyperpiesia, whether organic or functional, and the curious, scratchy, superficial murmur, so often heard in apparently perfectly normal hearts over the tricuspid area. This murmur is often to-and-fro in character. Dr. Strickland Goodall first drew my attention to it, and he suggests that there may be some connection between it and the milk-white patches in the pericardium so often found post-mortem in this region. Its comparative frequency in otherwise normal hearts would appear to rob it of any serious clinical significance.

Having ruled out organic disease, the estimation of the degree of stability of the cardiovascular system as a whole has then to be considered. There are many methods employed, centring chiefly on the effects of varying degrees of exercise on the blood-pressure, excellent in themselves, but having the fundamental disadvantage that the time occupied in their performance is too long. Those with which I propose to deal to-day are in routine use at the Central Medical Board in the examination for flying fitness, and while admittedly they are by no means perfect, they have the great advantage of simplicity, easy technique, standardization, and above all, speed.

(1) Pulse Response Test.—After the steady sitting pulse has been counted, the patient stands up, and the immediate rise in rate is noted. A second standing pulse

is taken as soon as the rate steadies again. The patient then puts one foot on a chair and stands upon it five times in fifteen seconds. The rate is then taken, and the time taken to return to the second standing pulse noted. The pulse is counted throughout in five-second intervals. A good response is: sitting pulse 72 per minute; standing pulse 84 and 72; after exercise 96; return to 72 in fifteen seconds. The sitting pulse alone, even if reasonably slow, is no criterion of fitness, as a sudden rise from 72 to 108 or 120 on standing is significant of splanchnic pooling. On the other hand, a sitting pulse of 96 which remains unaltered on standing and rises to 108 after exercise, shows relatively a higher degree of stability of the two. Physiological bradycardias, even as low as 48 per minute, are generally evidence of a high degree of cardiovascular stability. Their relative frequency in athletes, particularly in those indulging in long sustained effort such as cross-country work and rowing, has been frequently ascribed—often erroneously I think—to the effects of training. They are, in my opinion, constitutional, and such individuals have found from experience that they are capable of a higher degree of sustained physical stress than the average.

The average pulse of officers selected for permanent commissions in the Royal Air Force, as a result of their flying efficiency, is rarely above 72 and usually below, and practically all the well-known civil pilots have varying degrees of bradycardia, usually about 60 per minute, and training is not as a rule a factor in these cases.

Tachycardias may be purely transient, as a result of the excitement of the examination, and if the pulse comes down to say 84 per minute during it, and the rate after exercise to 120 per minute, it can probably be safely ignored in the absence of other signs of cardiovascular instability. Persistent rates of 96 or over, especially if accompanied by slight pyrexia up to 100°, are usually psychoneurotic in origin and rarely improve on re-examination.

(2) Blood-pressure.—The dial type of instrument tends to be unreliable, and requires frequent checking against the mercury-column type to ensure accuracy. A simple U-tube manometer with a large bore has been in standard use for many years in the Royal Air Force. Recently an American instrument known as the Baumanometer has come on the market, and it incorporates the broad-gauge tube. Estimations of systolic pressure alone rob the method of half its value. The technique of accurate reading of the diastolic with the stethoscope is difficult and requires considerable practice, but a very useful "tip" in this connection, devised by Group-Captain Flack, is to instruct the patient to tell one, as the mercury level is just below his systolic pressure and is falling, the instant he no longer feels the throbbing of the pulse in his arm. This point is the diastolic pressure. Three readings should always be taken and the pressure dropped between them, as a patient will frequently show a systolic pressure of 150 or over at the first reading which will come down to 140, or even 120, at the second or third reading. Such blood-pressures are purely emotional. The pressure should always be increased from 50 to 60 mm. above the point at which the beat is inaudible, as a blank area is occasionally met with above and below which the pulse can be heard, and gross errors may be made from time to time if this precaution is neglected. The normal blood-pressure of a healthy adult under 40 varies as a rule between 110 and 140 systolic and 65 and 85 diastolic. The pulse-pressure, i.e., the difference between the two, varies between 40 and 50. Small pulse-pressures in the normal individual, even down to 25 mm., are a most valuable sign of cardiovascular stability, and are usually associated with a slow pulse. The significance of pulse-pressure over 60 is a complex subject, but briefly, its significance depends on the relative heights of the accompanying systolic and diastolic pressures. A case of blood-pressure of say 125/55 nearly always shows other signs of cardiovascular instability, and has a small "fainting" margin. In three cases of this type at the Central Medical Establishment, the patients fainted during the test, and in each case a fall of 10-15 mm. was

noted in the diastolic pressure. A blood-pressure of 150/80, especially in the late "teens," is usually temporary and emotional, and is of small significance *per se*. A blood-pressure of 160/90, particularly if it remains relatively constant on further readings, is suggestive of an organic basis, and indicates the need for further investigation such as renal efficiency estimation.

It has been found at the Central Medical Establishment that rotation in a chair ten times in twenty seconds, the blood-pressure being taken immediately before and after, reveals the fact that the stable individual's blood-pressure does not change materially, that faintness and nausea accompany a fall in an already low diastolic, and giddiness a rise in a high diastolic. An increased pulse-pressure of over 10 mm. is unsatisfactory. The importance of this test in relation to flying is obvious. The type which shows no appreciable alteration usually has the slow pulse and small pulse-pressure previously referred to as signifying the presence of a stable cardiovascular system. The commonest factors in the production of an acquired high diastolic are focal sepsis—particularly from the teeth—and over-indulgence in alcohol.

(3) The 40-mm. test, as used in the Royal Air Force, consists of blowing a column of mercury to 40 mm. and holding it there as long as possible. The pulse is counted throughout in 5-second intervals. The duration of the test in the fit individual is over 60 seconds, and no appreciable alteration in the pulse should occur during the test. The many abnormal reactions that may occur, and their relative significance, render it impossible to discuss them in the short time left, but some electrocardiograms selected from a series taken before, during, and after the test illustrate some of the reactions met with. [Epidiascope illustrations.]

The conclusion arrived at then is that the characteristics of a stable cardiovascular system are a slow pulse, with a relatively slight increase on exertion, frequently a bradycardia, and a small pulse-pressure which again tends to remain relatively constant on exertion. What are the other factors found associated with it? First and foremost comes a stable nervous system, and a family history free from insanity or psychoneuroses. These individuals also have a power of quick recovery from illness not shared by the world at large. The type of case which takes weeks to recover from a severe cold or an attack of influenza rarely presents the above-mentioned characteristics.

Growth is a further factor of profound importance. The elaborate readjustment of the general body metabolism at puberty is a serious strain on the cardiovascular stability as a whole, and if this is followed by sudden rapid growth within the next year or two, it is rare to find no signs of its effects in the cardiovascular system generally. The tall, overgrown youth is rarely as physically fit as one of average size. Allowance can reasonably be made for this, as the same degree of stability cannot be expected after a recent burst of rapid growth. Slight enlargement of the thyroid is frequently found in these cases, and its significance can reasonably be regarded as less than it would be in a smaller individual whose system has not been required to bear the same degree of strain.

Lastly, a brief consideration of the reverse side of the picture, namely the functionally inefficient heart. It is met with usually in those of poor physique and of a nervous temperament. The family history frequently reveals the presence of psychoneurosis, and the nervous system is unstable. Enlargement of the thyroid is often found but is not constant enough to justify it as being regarded as one of the prime factors in the case. A history of rheumatism is occasionally obtained, possibly because it has left a legacy of concealed myocardial damage behind it. Acute illnesses and focal sepsis probably play a part in its production, but the most important underlying factor of the condition seems to be a constitutional one. The essential quality necessary to the successful athlete or airman—namely, an inherited tendency to a high degree of cardiovascular stability—is lacking in these

individuals, and rapid growth in their "teens," acute illness, and severe physical or mental stress, all tend to act as trigger-causes in the production of that clinical picture so well known throughout the Services as disordered action of the heart.

Discussion.—Dr. STRICKLAND GOODALL suggested that a more suitable title for the paper would have been "Cardiovascular Efficiency"—as a good deal of it was devoted to investigations of vasomotor reactions. Personally, he considered this the most important part of the communication, as in all probability an efficient vasomotor system was of more vital necessity in the Air Force than a "super heart," because the rapid change in altitude, position, emotion, etc., essential to flying, demanded rapid and perfect vasomotor adjustment. He regarded the pulse, 40 mm., and rotation tests as of supreme importance, and hoped later on to make a contribution on the 40 mm. test, which he regarded very largely as a test of right heart efficiency. He emphasized the importance of respiratory suction in an efficient venous return and in right heart filling, and entirely agreed with Wing-Commander Treadgold as to the relative importance of palpation and percussion. He pointed out that the only real sign of left ventricular hypertrophy was a heaving apex beat—he contrasted the apex beat in toxic, hypertrophied and normal hearts, and pointed out the value and importance of palpating the suprasternal notch. He agreed that the ortho-diagram was valuable, especially in connection with the great vessels, but very much doubted if one could always identify different parts of the shadow. The importance of auscultating all cases in three positions could not be overstated. He had done this as routine practice for over twenty years. In auscultating the aortic valve, three areas should be examined, the aortic base, pulmonary base and xiphoid. He was surprised to hear that 50% of Air Force recruits had a reduplicated first sound in the left lateral position—this was certainly a much higher percentage than occurred in gas works recruits. In his experience a definite canter rhythm was usually the first sign of myocardial infection or cardio-renal failure. He thought that probably the case of the young girl throwing multiple extrasystoles was one of toxic myocarditis. He would look with grave suspicion on any case that coupled the right heart with strain (40 mm. test).

Fleet-Surgeon W. E. HOME said that the Section might like to hear of a curious fact in medical history of which he had recently become aware.

He had previously always believed that the "effort syndrome" was a scientific advance due entirely to research during the war, and quite unknown before, and all his friends were of the same opinion. He had, however, found it described in Boerhaave's Lectures on Physic (London, 1747), vol. vi, p. 127. Boerhaave wrote (as translated and published after his death): "They who buy slaves count their pulse and respirations in a given time, and then order them to run. If now they find the respiration and pulse not much altered by that violent motion, they know that they are of a strong habit of body, but the more weak and morbid the slighter causes will alter the pulse, and those who are in a declining way towards death have their pulse twice or thrice as frequent as it ought to be when they exercise the body. This experiment is tried by the officers appointed to purchase soldiers for our Dutch colonies in the East Indies."

[1] Boerhaave (Leyden, 1668-1738).

Section of Surgery.

[*February* 5, 1930.]

DISCUSSION ON INTRATHORACIC TUMOURS.

Mr. A. Tudor Edwards: Considerable attention has been devoted during the last few years to the diagnosis and treatment of intrathoracic tumours. The increase in the number of cases of primary malignant disease occurring in the thoracic cavity has led to repeated debate as to whether it is a true increase or is due to the more exact methods of diagnosis now available. The greater number of cases of benign growths reported in the literature suggests that the diagnostic factor is at any rate partially responsible, as it cannot be supposed that there has been an actual increased incidence of these tumours.

Tumours may be divided into three classes—(1) Mediastinal, (2) Pulmonary, (3) Pleural. This classification refers to their origin only, as many mediastinal tumours grow outwards into the lung itself or between the lobes. Certain of the so-called pleural tumours arise from structures immediately outside it, such as fat, nerve tissue, and bone, and project into the pleural cavity, covered only by a modified layer of the membrane.

(1) Mediastinal Tumours.

The benign tumours are intrathoracic thyroids, dermoids, and teratomata. Aneurysms occasionally give rise to difficulty in differential diagnosis.

The primary malignant tumours consist of sarcoma, carcinoma of the thymus, and lymphadenoma. Secondary carcinoma in the mediastinal glands results from carcinoma of the bronchus, lung, or pleura, and from extrathoracic regions, most commonly from carcinoma of the breast.

(*A*) *Benign Mediastinal Tumours.*

Intrathoracic goitres tend to remain localized to the superior mediastinum and, possibly owing to their attachments at the root of the neck, rarely migrate outwards towards the pleural cavity. They therefore give rise to symptoms characteristic of benign growths situated in the superior mediastinum. Dermoids and teratomata, on the other hand, tend to spread laterally, passing outwards towards the parietal pleura, and sometimes between the lobes of the lung.

Symptoms.—The most characteristic early symptom of intrathoracic goitre appears to be dyspnœa. The type of dyspnœa varies, being more or less constant in some cases and definitely paroxysmal in others. As the tumour enlarges there is gradual obstruction to the venous return, which results in cyanosis of the skin of the head and neck, and in more advanced cases there is considerable dilatation of the veins at the base of the neck and over the sternum.

In one case only have I seen evidence of pressure on nerves.

In addition to the symptoms of intrathoracic tumour, symptoms of toxic goitre may be present. In two patients upon whom I operated for the removal of substernal goitres toxic symptoms were very marked; it is interesting to note that

one of these patients had been treated for aneurysm for nine months previous to operation.

Physical signs of intrathoracic goitre consist of an area of dullness of varying extent, on percussion over the sternum, and of enlarged dilated veins overlying the same area. The former sign is not present in the rare cases in which the goitre is retrotracheal.

X-ray Examination.—Shows a well-defined opacity in the upper substernal area. A lateral skiagram offers difficulty in this region, but oblique views show the tumour to be situated anteriorly. Diagnosis may not be possible from a similarly situated dermoid.

Mediastinal dermoids and teratomata in my experience rarely, if ever, give rise to symptoms due to their mediastinal position. When they extend outwards two groups of symptoms may be encountered. The first group is associated with irritation of—and finally rupture into—a bronchus. Irritation causes a non-productive cough without signs of pulmonary changes. Eventually the cyst perforates into the bronchus and portions of the contents, e.g., hair, may be expectorated. The incidence of infection gives rise to signs of pulmonary abscess, such as pyrexia and offensive purulent expectoration. In certain cases, the pressure of the tumour on the lower lobe bronchi results in the establishment of bronchiectasis. In the second group, however, the tumours appear to extend outwards without symptoms until the pleura is reached, the first evidence of their presence being the onset of pleurisy. Dullness on percussion will be associated with a friction rub and an absence of breath sounds over the area of the tumour.

X-ray Examination.—The results will vary according to the size of the tumour. In all cases the outline of the tumour, unless infection has supervened, will be clearly demarcated. The tumour is generally rounded or oval, and if bone or teeth are present they may show as denser opacities. Skiagrams following induction of artificial pneumothorax will help to distinguish these tumours from intrapleural tumours, as intrapleural tumours are seen to be free from the collapsed lung, whereas teratomata appear to be buried in it.

Treatment.—Intrathoracic goitres should be removed as soon as symptoms of interference with respiration supervene. Smaller tumours extend downwards in a continuous mass from a goitre normally situated and can be removed through the usual curved cervical incision. After blunt separation from the capsule with the finger, they can be dislocated into the neck and easily removed. In the case of larger tumours—and especially when there is little or no visible connection with the thyroid gland in the neck—it will be necessary to split the sternum in the middle line down to the third interspace. The sternum is divided transversely into the interspace on one or both sides, according to the exposure required. Retraction of the two portions laterally will give adequate exposure for tumours of considerable size. The capsule is opened and the tumour enucleated. The divided portions of the sternum are drawn together with catgut and the wound is sutured; a rubber-tissue drain is inserted into the suprasternal notch and left for twenty-four hours, to allow evacuation of effused serum.

Dermoids and teratomata, when localized to the mediastinum, can be approached by the same route, but in my experience they should be exposed through the pleura. Localization by skiagrams of the exact position of the tumour from different directions should enable the surgeon to decide whether to open the chest through an anterior or posterior incision. In general, the large tumours will be exposed by a posterior incision and the smaller ones by the anterior route.

Operation.—The following thoracotomies will allow free exploration of all intrathoracic tumours:—

(1) Anterior Exposures.—A curved incision is made through the skin and superficial tissues. In the female, the incision is made around the lower border

of the breast, which is reflected upwards. The pectoralis major is split and the chest opened in the third or fourth intercostal space. Retractors are inserted and the tumour exposed. When wider exposure is required the costal cartilages of the rib, or ribs, above can be divided and a portion of the chest-wall thereby raised. The lung overlying the tumour may require incision, or the separation of the interlobar space may be necessary.

(2) Posterior Exposure.—The posterior operation allows considerably more room for manipulation within the thoracic cavity. A curved incision is made along the vertebral border of the scapula and is continued outwards along its inferior angle. By abduction of the upper limb the scapula is rotated outwards and the chest is opened through any intercostal space from the fifth to the seventh, according to the requirements of the case. Further exposure can be obtained by resecting a small portion (1 in.) of one or two ribs above, and enlarging the pleural opening to this limit.

After removal of the tumour, the chest is closed air-tight by approximation of the muscular layers. I have found it unnecessary to use percostal or pericostal sutures, and it is invariably impossible to see the opening in the pleura. A loose suture is put in the intercostal muscles in order to prevent them falling inwards, but with no intention of air-tight suturing. Strapping is applied to the affected side of the chest after operation, and aspiration is performed as often as necessary.

I have operated upon seven true intrathoracic goitres. Of these, three were so large as to require division of the sternum, while the other four were removed through the superior aperture of the thorax. All the patients complained of shortness of breath, and two had been treated as cases of asthma for three or four years. There was one post-operative death, the patient suffering from toxic signs of goitre, and post-mortem examination showed considerable enlargement of the thymus.

Seven cases of teratomata or dermoids have been operated upon, in two of which rupture had occurred and secondary infection intervened. Considerable variations in size and structure have been encountered. The largest consisted of a cyst containing four and a half pints of sebaceous material and a large mass of fleshy tissue at the root. The majority have been solid, with only small quantities of sebaceous material in multiple cavities. The only death occurred in a patient with a solid teratomatous tumour the size of a fœtal head.

A rare type of mediastinal tumour has also been operated upon. It was a large cyst containing just over one and a half pints of fluid almost saturated with cholesterol and arising from the pericardium. It was successfully removed and the patient was well four years later.

(*B*) *Malignant Mediastinal Tumours.*

Only very rarely will operation be possible, and even more rarely will complete freedom from recurrence follow. In one case, a primary lymphadenoma of the thymus, operation was undertaken and the thymus removed. The patient survived operation and was in fairly good health for several months after operation.

The majority of cases of sarcoma of the mediastinum are inoperable, but should be treated by radium, either externally applied or, when the tumour is not too vascular, by the insertion of seeds or needles. Personally, I am disappointed with the results of deep X-ray therapy. Even in cases of lymphadenoma, which often disappears rapidly when this treatment is first instituted, recurrence is the rule and the tumour then appears to be insensitive to the rays.

(2) Pulmonary Tumours.—(*A*) *Benign.*

Benign tumours of the lung are extremely rare. Fibroma and lipoma of the bronchus have been described and, in addition, chondroma and osteoma in the lung. Dermoids of the lung have been recorded, but it is probable that they have originated

in the mediastinum and burrowed into the lung. The most common cyst in the lung is the hydatid, which may be single or multiple.

Signs and Symptoms.—Cough and expectoration, occasionally associated with pain when the tumour is near the lung surface, appear to be the common symptoms. When the tumour arises in the bronchi, hæmoptysis may occur.

I have only operated upon one benign cyst of the lung. This was non-parasitic and was removed with the adjacent portion of lung, as its benign nature could not be determined before removal.

(*B*) *Malignant Pulmonary Tumours.*

Primary carcinoma may arise in the bronchus or in the alveolus. The bronchial type is much more common and its origin is generally in the larger bronchus, near the hilum. Bronchial carcinomas are of two histological types, the squamous-celled carcinoma arising as a result of metaplasia in the bronchial mucosa, and the cuboidal acinar type containing a quantity of mucoid material and arising from the mucus-forming cells of the bronchus.

The central carcinomata arising in the alveolus are generally squamous-celled, but endotheliomata appear to arise in the same position, possibly from vessels or lymphatics.

Sarcoma is much rarer than carcinoma, and the two chief varieties are the spindle-celled type and the peribronchial infiltrating sarcoma composed of small round cells.

Signs and Symptoms.—(*a*) In cases of bronchial carcinoma, dyspnœa appears to be the earliest and most predominant symptom. Occasionally hæmoptysis may initiate the history, but in many cases a febrile attack—diagnosed as influenza—is the first evidence of chest disease. Later symptoms vary; some cases develop an effusion; in others the patients appear to enjoy fair health for some months after the diagnosis is obvious. In most cases the physical signs are those of atelectasis of the lobe communicating with the affected bronchus. The diagnosis may be confirmed by the introduction of lipiodol, which shows an irregular blocking of the involved bronchus in the skiagram subsequently taken. Bronchoscopy, with removal of a portion of the growth, will confirm the diagnosis.

(*b*) The central carcinomata may give rise to hæmoptysis or cough associated with mucoid expectoration. X-ray examination shows an irregular opacity without evidence of surrounding lung reaction, its localization in the lung tissue can be shown by indueing pneumothorax and re-examining with the X-rays. When there is secondary involvement of glands in the neck, these should be removed under local anæsthesia for histological examination.

The later stages of all types of malignant disease in the lung may be associated with the presence of a pleural effusion, either serous or hæmorrhagic.

(*c*) Endothelioma occasionally arises as a central growth in the lung and can only be distinguished microscopically from carcinoma.

Treatment.—Bronchial carcinoma rarely allows of radical extirpation, owing, firstly, to its late diagnosis, due to lack of symptoms in the early stages, and secondly, to the early involvement of the mediastinal gland.

On rare occasions papillomata showing early malignant changes have been successfully removed through the bronchoscope. Recently I have had the opportunity of removing a tumour, the size of a plum, from the upper lobe of the left lung. This tumour was arising from a bronchus and was proved histologically to be a carcinoma.

These cases are exceptional and merely serve as contrasts to the commoner types.

Radiotherapy.—With regard to deep X-ray therapy, I have yet to see improvement, much less cure, in any case of bronchial carcinoma. Radium as a surface application, in greater or lesser doses, has also been disappointing in my hands.

In a certain number of cases I have used radon seeds, and, although I have not yet seen a definite disappearance of the growth, there has been such distinct improvement as to warrant its further trial. The seeds should not be inserted in a haphazard manner through the chest-wall, but only after full exposure of the tumour. In another case, radon seeds in a special container have been inserted into the bronchial lumen, and have been retained by the patient for five days on each of two periods. The result is yet to be seen.

Central carcinoma and endothelioma offer a much more favourable group for operative treatment. Three cases have been submitted to operation: one of squamous-celled carcinoma and two of endotheliomata.

There was one post-operative death due to reactionary hæmorrhage from an intercostal artery, the other two patients recovered from operation. In one case complete lobectomy was performed fourteen months ago and the patient is well to-day; the other patient survived after subtotal lobectomy, but died from recurrence five months later.

In one case in which a sarcoma was removed, the patient died from pneumonia in the opposite lung nine days later.

Secondary Malignant Disease in the Lung.—Rarely will any form of treatment be of value for secondary deposits in the lung, but partial pneumectomy was performed in one case of secondary myeloma (primary in the fibula) in the left upper lobe. This patient has survived operation two and a half years and is still well.

(3) Pleural Tumours.—(*A*) *Benign.*

The greater number of tumours described as pleural, probably arise in structures immediately adjacent and develop inwards. Thus lipoma, fibroma, chondroma and ganglion-neuroma have been described. Hydatid cysts also arise in this situation.

These tumours give rise to symptoms of pain and irritative cough, and are accompanied by signs of localized dullness and absent or diminished breath-sounds over the area of the tumour. X-ray examination confirms the diagnosis of tumour and its clear outlines differentiate it from infiltrating tumours. Radiography, subsequent to pneumothorax, distinguishes these tumours from those arising in the pulmonary tissue.

Treatment.—Surgical removal should be advocated as soon as the diagnosis is made if the general state of the patient permits. All benign intrathoracic tumours destroy life eventually by pressure on important structures, and early removal permits of successful results. One patient from whom a chondro-sarcoma was removed six years ago is still living without recurrence, as is another, four years after removal of a lipo-chondro-sarcoma. One patient died after removal of a large fibroma, but post-mortem examination disclosed cardiac disease.

(*B*) *Malignant.*

Endothelioma and sarcoma are encountered, arising in connection with the pleura.

Endothelioma may be localized or diffuse, the latter being more common. Localized thoracic pain is the common symptom. The physical signs are those of pleural effusion, which, on aspiration, may be serous in the early stages, but is always hæmorrhagic later. Removal of the fluid and replacement by gas will allow of thoracoscopic examination.

Treatment.—The localized type may be removed if diagnosed before secondary deposits are evident. In the generalized form, treatment by radium should be instituted. In one case a localized sarcoma was successfully removed, but the patient died eighteen months later from paraplegia, as a result of secondary deposits in the spine.

CONCLUSIONS.

Modern methods of investigation have made the diagnosis of intrathoracic new growths much more exact. These methods entail:—

(1) Methodical X-ray examination of the chest from antero-posterior, lateral, and oblique aspects.

(2) Another series of skiagrams after the induction of artificial pneumothorax, or gas replacement of any effusion present.

(3) In certain cases, X-ray examination following lipiodol filling of the bronchial tree.

(4) The introduction of the thoracoscope into a pneumothorax cavity for visual examination of the superficial surface of the lung and pleura, and tumours arising from or projecting into the pleura.

In spite of these advances, there will remain a proportion of cases in which exact diagnosis will be impossible, and in these, exploratory thoracotomy should be performed. With certain precautions this operation is of no greater severity than exploratory laparotomy, and, in fact, the convalescence afterwards is shorter. By this means certain tumours which were primarily thought malignant have proved to be benign and have been successfully removed, and others, definitely malignant, have been found operable.

This series includes twenty-seven operable tumours.

It should be borne in mind that benign intrathoracic tumours may destroy life by pressure upon vital structures within the thorax.

Mr. W. H. C. Romanis: I will confine my remarks to the four classes of which I have had experience: goitres, dermoids, hydatids, and malignant growths of the lung.

We are all accustomed to see cases of Graves's disease with a large mass of thyroid tissue extending behind the sternum. We also, more rarely, see the plunging goitre, which "lives" in the neck but moves up and down into the chest when the patient coughs or swallows. Neither of these is a true retrosternal goitre; the real thing is very definite: a large mass of thyroid tissue, right down inside the chest, with, sometimes, no visible connection with whatever thyroid tissue there may be in the neck. In the diagnosis of this condition, the important point is to remember its possibility. When a skiagram shows a rounded dense shadow below the sternal notch, if we remember that it may be a retrosternal goitre, we are not likely to mis-diagnose it. Incidentally, it is the only form of intrathoracic tumour which moves up and down when the patient swallows, as can be seen on the X-ray screen.

Occasionally we see patients who obviously have Graves's disease but there is no enlarged thyroid palpable in the neck. Sometimes these patients have a large retrosternal goitre, and X-ray examination will make it obvious.

These retrosternal goitres can usually be easily removed, but sometimes removal is very difficult. Only once have I found it necessary to split the sternum. I do not, however, think there is any objection to splitting the sternum if it will make the operation much easier. Many of these goitres can be removed with the handle of a blunt instrument, simply by pulling them up. This demands some courage, because this is not a region in which to pass blunt instruments blindly, but it is usually possible to drag them up, as the blood-supply of these swellings nearly always comes from above, and they do not tend to form attachments to the big veins. There is also a manœuvre which is often most helpful, and that is disarticulation of the clavicle on whichever side the growth projects most, accompanied by section of the first costal cartilage; this may give the increased room which will make all the difference between a difficult and an easy operation.

As to dermoids, one of the most interesting points about them is the variety in their first or principal symptom. I remember that the first one I saw was diagnosed by the late Dr. J. J. Perkins in a girl aged 21, who had as her only symptom, attacks of recurrent pleurisy with effusion. Dr. Perkins diagnosed a dermoid cyst, and

said where it lay. At operation there was a large dermoid lying in the posterior mediastinum which we easily removed. In other cases these dermoids become infected and give rise to symptoms of suppuration in the chest. Sometimes the main symptom is the bringing up of sputum owing to the cyst having ruptured into a bronchus, and it may not be for some time that hair appears in the sputum and establishes the diagnosis. Pressure on important structures is not common, but I have seen one case in which there was gross interference with the heart's action.

As to removal of these dermoids—and most people agree that removal is the only treatment—I have little doubt that the best approach is from the side, by making a large incision between two ribs. There is no need to take out a rib, if Tuffier's rib-spreader is used. By excising one rib the operation may be made easier. The pleura is opened and the dermoid cyst can then be approached satisfactorily. This is a class of operation in which every case has been either very difficult or very easy; I have not encountered a dermoid which was just moderately difficult to remove. They may be very adherent or they can come out easily with very little dissection. In one or two cases it was difficult, or even impossible, to remove all the cyst, because it disappeared among the great vessels above or under the arch of the aorta, and on two occasions I have had to take out the greater part and leave behind some of the cyst wall buried in one of the deep portions of the thorax. Two of these patients have gone on well for three and four years without any signs of the fluid re-accumulating. Apparently, therefore, leaving behind a portion of the lining does not necessarily lead to a recurrence of the condition.

Hydatid cysts are, of course, a rare form of tumour in this country. It is the practice among Australian surgeons to marsupialize these cysts and bring them to the surface, but I have always attempted to remove the endocyst. The chief precaution is to remember that it is just as serious to let a quantity of hydatid material escape into the pleura as it is to contaminate the cavity with pus. Such an operation therefore starts out on the same lines as an operation which aims at opening an abscess in the lung, because something must be done to shut off the general pleural cavity. Although in the case of an abscess of the lung it is probable that the general cavity will be already adherent or shut off, it is not likely to be so in the case of hydatids, so that the two layers of pleura must be fixed together before attempting to remove the endocyst, which is then easily done. Very little in the way of ectocyst occurs in the lung, and very little fibrous tissue is found round the cyst, and this fact gives an excellent prospect to operative removal, because expansion of the lung afterwards occurs more easily. Removal of hydatid cysts of the lung is a most satisfactory operation, because these cysts are easily removed, and the patients do well afterwards. Years ago I was warned by a physician that it was dangerous to aspirate a hydatid cyst for the purpose of diagnosis. At the time I did not quite believe it, but later I saw an accident happen when a needle was inserted into a hydatid; the cyst burst, and discharged a large quantity of watery fluid up the patient's bronchi. The patient was not drowned, but was nearly so. The warning therefore seems to have a sound foundation.

As to malignant disease of the lung: the percentage of operable growths which any surgeon encounters among the total number he sees, is at present very small, and I most strongly endorse Mr. Tudor Edwards' observation that the only possibility at present of meeting more operable cases lies in early exploration in all doubtful cases. Exploration of the chest, made between two ribs without taking out bone, is not any more serious than is exploration of the abdomen, and it is much less serious than exploration of the head. Until this early exploration is undertaken more often we shall not encounter many cases of growths of the lung in an operable state.

Radium treatment is at present in its infancy. I am not altogether a radium enthusiast, but we have had the opportunity of trying radon seeds in some cases, and,

so far as one can see, it has as beneficial effects on certain growths of the lung as it has on certain growths of the breast or of the tongue. I have one case at present under care which is a surgical failure but a radium success. It is that of a man with a growth in the lung, into which, through a large exploratory opening in the chest—which is the only way to do it—we put thirty radon seeds. That was some time ago. There was a certain amount of suppuration, and the wound gaped widely open. The lung remained collapsed, and there is still a large hole through which the pleura and the greater part of the lung can be seen, but the growth has completely disappeared. It will, however, be many months before the patient recovers from the suppuration. I think there will be a fair number of successes with radium in cases of growth of the lung. The use of radon seeds obviates the difficulty of removing the radium afterwards.

With regard to exploratory thoracotomy and the methods of removing most of these tumours, one procedure is essential, both to render the operation easier and to make the diagnosis more certain; and that is, the production of an artificial pneumothorax. Before opening a chest for removal of any of these intrathoracic tumours, except retrosternal goitres, it is a great help to have the lung collapsed, and as we are not dealing with a tuberculous or otherwise infected lung, pneumothorax can be produced with great rapidity, and may safely be carried out in two stages two days beforehand. More room is thus obtained for exposure of the growth than if we only allow the lung to collapse at the time of the operation, when the chest is opened.

Dr. L. S. T. Burrell: If the very rare forms of intrathoracic tumour are excluded, the following may be taken as a working classification: (A) Benign, including (1) Fibroma; (2) Dermoid. (B) Malignant, including (1) Endothelioma of pleura; (2) Carcinoma of lung; (3) Sarcoma of mediastinum.

Symptoms.—The early symptoms are: (1) Pleural effusion which is especially common in cases of endothelioma of the pleura; (2) Pressure symptoms usually due to collapse of lung and to pressure on a bronchus, which may develop suddenly so that it resembles pneumonia, or to pressure on the vessels, producing enlargement of the superficial veins and possibly œdema of an arm or side of the face; (3) Hæmoptysis—this occurs especially in tumours of the bronchial tubes. In malignant cases it is slight, but it may be copious in cases of fibroma.

Diagnosis.—Unlike the condition in tuberculosis, the general health of the patient usually remains good. If a bronchus is obstructed, signs of collapsed lung appear but in many cases the diagnosis can be made only by X-ray examination.

The effusion in cases of neoplasm is often blood-stained, and excess of endothelial cells in the pleural fluid is suggestive of neoplasm.

Occasionally the shadow shown in the skiagram is due not to the growth but to the associated collapsed lung, so that a large shadow does not of necessity indicate a large or inoperable tumour. It is important to have a lateral skiagram taken as well as an antero-posterior one.

The injection of lipiodol into the bronchial tubes before the X-ray examination shows clearly where the tube is obstructed and assists in the differential diagnosis between a pneumonic condition and one of collapse.

In certain cases when there is effusion, examination through a thoracoscope will enable the tumour to be seen in the pleura or extending from the lung. If there is no effusion it may be helpful to induce a temporary pneumothorax through which one can make a thoracoscopic examination.

Carcinoma of the lung is by far the most common of the malignant tumours. It usually begins in the bronchial tubes and may invade the mediastinum and a large portion of the lung. Many of the growths which were formerly called lympho-

sarcoma are now known to be carcinoma, although genuine cases of lymphosarcoma of the mediastinal glands do occur.

Metastases from carcinoma of lung may occur in any part of the body, but the most frequent sites for them are: Liver, 40%; bones, 20%; distant glands, 12%; kidneys, 12%; spleen, 10%.

Treatment.—The only chance of saving the patient is to remove the tumour by surgical operation. In certain cases of sarcoma or when the glands are enlarged as a result of lymphadenoma, improvement may follow X-ray therapy, but, in my experience, recurrence invariably takes place.

I have never seen a case of intrathoracic tumour in which radium treatment has been of any assistance; possibly in the future it may give good results. At present, however, I must emphatically insist upon the danger of delaying surgical treatment whilst other methods are being tried. If operation is possible, it should be performed at once; if the case is inoperable, this and this only will justify other methods of treatment.

Five cases recently under my care have been successfully treated by surgical operation. In two of these the condition was fibroma of the bronchial tubes; in both, the tumours were removed through a bronchoscope and both patients made an uninterrupted recovery. Of the three other cases, one was a case of dermoid cyst, and another of a bronchial carcinoma which was removed by open operation; the patient so far is doing well. In the last case, which was one of fibroma of lung, the lower lobe, including the tumour, was removed and the patient remains well more than a year later.

Dr. F. G. Chandler: Primary malignant tumours of the chest are common, and, I believe, have always been so. There has been much discussion of late as to whether they are becoming more common. The evidence produced is, to my mind, fallacious. Their more frequent recognition has coincided with the radiographic method of diagnosis. Diagnosis of chest diseases generally has become more accurate during the last twenty years. It is a fallacious argument to say that cases are appearing much more frequently on the post-mortem table. Cancer of the lung is being more talked about and more thought of. Tentative diagnoses, therefore, are made more frequently, and cases are consequently sent into hospital more frequently, and it is here alone that the post-mortem examinations are made. It would be as logical to say that innocent tumours had become more common since the publications of Jacobæus.

Primary malignant growths may be exceedingly difficult to diagnose in the early stages, or in later stages, by reason of their breaking down and simulating abscess or because of fluid or pus in the pleural cavity. The symptoms are either pressure symptoms due to pressure on veins, trachea, bronchi or nerves; lung or bronchial symptoms, such as cough, hæmoptysis or simply malaise and progressive loss of weight and condition; or the illness may begin like an attack of broncho-pneumonia —fever, hæmoptysis, a patch of consolidation.

The surest way to diagnose is to make: (1) an X-ray examination, as soon as possible, before fluid in the pleura or secondary changes in the lung distal to the tumour have obscured the view; (2) a bacteriological examination to exclude tubercle bacilli; and (3) a bronchoscopic examination. Physical signs take a very subsidiary place. Paralysis of a phrenic or of a recurrent laryngeal nerve is strongly suggestive of a growth. But sometimes, having excluded tuberculosis, all that one can say is that this patient is deteriorating so rapidly that growth is the probable diagnosis.

When there is dullness and X-ray opacity, the exploring needle may be diagnostic. The firm resistance of the tumour may be pathognomonic. Sometimes, but not usually, secondary glands will help the diagnosis. Occasionally the growth will break down, forming an abscess. This, if the patient was not seen in the

early stage, may make the diagnosis very difficult, but when doubt exists we should act on the principle that when the diagnosis rests between a curable and an incurable condition, the curable one should be diagnosed. It is better to operate on a hopeless growth than to neglect a treatable abscess.

A pleural effusion is common over a growth. Help may be obtained by replacement and subsequent radiography. The same applies to an empyema. I remember a case in which a chest was explored and—at first clear fluid—and then, as the needle was pushed further in, pus—was obtained. This indicated fluid over a lung which contained pus, a not uncommon condition with malignant growth. Another difficulty is the slow course of some cases of primary carcinoma of the lung.

I have expressed the matter rather from the consultant's point of view. The general practitioner has another important aid in diagnosis, namely, the course of the malady after the first symptoms. The course is perhaps unusual for one of the conditions suspected. This should suggest further investigation. Mistakes are made largely because this investigation is not made or because malignant growth is not thought of. The investigation must include an X-ray examination. A word of warning is, however, urgently necessary. Just as it may be difficult clinically to distinguish between an abscess and a growth, so it is difficult to distinguish between a growth and other conditions, in the skiagram. I have known serious mistakes made because this is not recognized. I defy anybody to say what this rounded mass is on a skiagram taken by Dr. Harrison Orton [slide shown on screen] from the radiological appearance, without knowing the clinical history. It looks like an enormous innocent tumour or a dermoid. It is almost certainly an encysted collection of fluid remaining after the termination of an artificial pneumothorax. The patient is perfectly fit and has been so for ten years. The condition shown in the next skiagram (exhibited) was interpreted as a pyo-pneumothorax. Clinically, the case was one of carcinoma of the lung. With the exploring needle a tough resistant mass could be felt. The patient did not deteriorate so quickly as was expected, and six months later another skiagram was taken. The radiologist persisted in his diagnosis. An exploratory operation was performed and an inoperable carcinoma was found. The skiagram shows very well the irregular thickening of the inner wall of the cavity which Mr. Morriston Davies describes in his recent book, as distinguishing a necrotic growth from abscess.

Treatment.—Inflammatory tumours need little comment. Rare though it is, apparently, gumma must not be forgotten. I have shown a slide of a gummatous mass in the mediastinum which had caused pressure-symptoms and enlarged veins over the chest for eight years. A diagnosis had never been made and the man died from cerebral complications shortly after admission to Charing Cross Hospital. Lymphadenoma, even though large and primary in the mediastinum, is probably best treated by arsenic, X-ray therapy and radium. By a heroic operation Mr. Tudor Edwards removed successfully an enormous lymphadenomatous mass from a young patient, and she died from recurrence of the disease in other parts. She had no symptoms before the mass had become very large, and I doubt if any method of treatment would have saved her. In such a case there is no question of early diagnosis because the patient does not seek advice early, and this is often a difficulty with regard to intrathoracic tumours.

Innocent tumours should be treated surgically, if causing symptoms and growing in size; the same observation applies to mediastinal thyroids.

The treatment of intrathoracic malignant disease resolves itself into the following methods: X-ray therapy, radium therapy, surgical removal, and the relief of symptoms. No other methods have at present any serious claim. No treatment, unfortunately, can promise a cure. In 1927 I published an investigation of 120 cases of primary malignant intrathoracic tumours, of which half had been treated by X-ray therapy. In only four were the patients still alive. Three of these were

certainly not cases of malignant disease. The fourth was almost equally certainly a most definite case of sarcoma. There were large masses in the mediastinum and a bilateral pleural effusion. A gland removed from the neck was histologically a lymphosarcoma. The patient—a woman aged 25—was admitted to St. Bartholomew's Hospital in 1923, under the care of Sir Thomas Horder and Dr. Gow, and was treated by Dr. Finzi. She made a perfect recovery. Four years later she was in perfect health, and a skiagram showed her chest to be normal (slides shown). This is the only case known to me in which a truly intrathoracic malignant tumour has been cured by X-rays, and has remained cured. I cannot help thinking that this deplorable scarcity of cures by X-ray therapy is due in some measure to lack of knowledge of proper dosage and inadequate technique.

Radium.—I have had radium inserted into the tumour, but have no success in my series of cases to record. I feel, however, that with improved technique we ought to get better results. The problem resolves itself into the questions of early diagnosis, the surgery of approach, and the method of applying the radium.

Surgical Removal.—The greatest hope in a lung carcinoma would be early removal. Success will depend on the operability of the growth and on the skill and gentleness of the surgeon, and equally on the skill of the anæsthetist. As a rule symptoms do not occur, or a diagnosis is not made until the mediastinal glands are involved. Earlier investigation and the more frequent employment of bronchoscopy may help the surgeon in the future. Carcinoma has been removed surgically by complete or partial lobectomy. Unfortunately in some successful cases there have been metastases, an example of which I show. The tumour was a secondary hypernephroma. The patient died a few months after operation from metastases in other parts of the body.

The Relief of the Symptoms.—If we cannot adopt active treatment, we can at least relieve suffering. When the relatives say to me: "then nothing can be done, doctor?" I reply, "yes, a great deal can be done; something that will make all the difference between comparative comfort and a death possibly of agony; this is not nothing." They can appreciate this and are grateful. So often I find that inadequate doses of anodyne are given. Here, if anywhere, we surely must endeavour to ensure euthanasia. I believe that the first thing to do, if surgery, X-rays and radium fail, or are not indicated, is to accustom the patient to some form of opium—tincture of opium, nepenthe, heroin, omnopon, etc. This will often overcome the common idiosyncrasies to opium and enable large doses to be taken when they become necessary. The dose then is that necessary to relieve. There is no other criterion of dosage. I, personally, let the patient have the medicine or the tablets at his bedside. Other things that may afford relief are hydrocyanic acid (dil.), cocaine ¼ gr. (or more) by mouth and by hypodermic injection, allonal and possibly injections of novocain as a local anæsthetic if the pain is superficial. Nerve blocking might be tried. But the chief thing will be opium and this should give relief. So many people, however, react badly to it that we must endeavour, as quickly as possible, to establish a tolerance.

In conclusion: We must be quite frank with our patients if there is the slightest chance for them; in certain cases the boldest surgery and big risks are justifiable, and many a patient, if he knew the truth, would gladly coöperate in a forlorn hope and willingly take the risk. We, knowing both the truth and the risks, may think that we should prefer to die, but in my experience the stricken doctor clings as earnestly as his patient to the forlorn hope.

Mr. A. D. Wright said: The subject of this discussion is so vast that more profit will be gained by confining my remarks to the commonest condition found, namely, irremovable carcinoma of the lung. The other conditions are, comparatively speaking, rarities, but this condition is encountered almost every week. The

commonest symptoms that I have found in this condition are: (1) fits of dry coughing; (2) prolonged pyrexia; (3) cyanosis, in association with the coughing attacks; (4) engorgement of cervical veins.

There is only one treatment available at present for these growths and that is radium emanation implanted into the tumour in the form of seeds which do not require subsequent removal.

The operation of implantation as usually done is fraught with danger of trans-pleural implantation. A stout trocar and cannula is plunged into the growth and the seed implanted; on withdrawal of the trocar blood wells out of the puncture, certainly carrying with it cancer cells which fall to the bottom of the pleural cavity and, lying there beyond the range of adequate radiation, become the starting point for a recurrence.

I have devised a method of overcoming this flaw in the technique.

(*a*) The trocar and cannula is of the smallest possible gauge.

(*b*) The cannula is insulated along most of its length with Bakelite.

(*c*) The trocar and cannula is inserted up to the insulation, and the seed, glued on to a stilette with paraffin wax, is introduced into the cannula after withdrawal of the trocar.

(*d*) The diathermy current is turned on for five seconds and produces the following results: (i) coagulates all cancer cells along the tract; (ii) renders the puncture wound dry; (iii) melts the paraffin wax and releases the seed into the growth.

Another point I found of value on one occasion was the creation of a bronchial fistula in a case of carcinoma of the mediastinum in which the patient was dying from asphyxia due to tracheal involvement. The operation was carried out in two stages, the first to create adhesions between the pleural layers, the second to open a main bronchus by means of the diathermy knife. Between the two operations the patient was kept alive by producing an extensive oxygen emphysema of the subcutaneous tissues. This patient lived for seven months, breathing through the bronchial fistula. This manœuvre might be of value in treatment under the radium bomb or X-rays when, because of the dyspnœa, great difficulty is found in getting the patient to lie flat for the treatment.

A patient now shown to the Section illustrates the phenomenal effect of radium on carcinoma of the lung. His history is as follows; Admitted to St. Mary's Hospital on November 11, 1929. In June, 1929, he had noticed a swelling in the neck, and the cough—which had been troubling him for six months previously—had now become so severe that in some of the attacks he fainted. Lately, during these attacks, such a severe cyanosis had developed that he was black in the face before finally becoming unconscious; the unconsciousness persisted for from three to five minutes as a rule. On account of dyspnœa and coughing he had, during the last two months, slept only in a sitting posture. On the day before admission he had become unconscious from asphyxia on ten occasions.

The condition on admission was characteristic of intrathoracic growth; the face was blue and engorged, and on the right side of the neck above the clavicle was a large fluctuant tumour which doubled in size when the patient coughed, reaching the size of an orange; the swelling was non-resonant and consisted of tremendously engorged veins. The chest was dull over nearly all of the right side, with bronchial breathing in front and signs of fluid behind. There was no sputum. A skiagram showed fluid and a circumscribed shadow in the upper lobe, resembling a new growth.

On November 23, 1929, an exploratory thoracotomy was carried out through the third right interspace from the front, after dividing the pectoralis major and removing a portion of the third rib. The tumour was found to be irremovable, as it was continuous with the mediastinal structures over a large area, and was about the size

of a child's head. The pleural wound was closed by stitching the pectoralis major over it. Fourteen days later the thorax was re-opened and 100 millicuries of radon in 33 seeds inserted. The length of the seeds was 0·5 cm. and the screenage 0·2 mm. of silver.

The patient did not look back after this, and was discharged a month later with no signs of growth radiologically or clinically, and completely free from the distressing cough. He is now back at his employment of butler.

Dr. James Maxwell said he wished to give, briefly, from the pathological point of view, the result of his examination of the notes of 184 cases of primary bronchial carcinoma collected at St. Bartholomew's Hospital and the Royal Chest Hospital.

These could be divided into four groups, depending on the site of origin of the growth and its method of spread. In the first group, which comprised only 6% of the whole, the growth started in a main bronchus at the root of the lungs and formed a tumour in the hilum. Tumours of this group were not liable to metastasize early and therefore held out the hope of some success in treatment. The second type (20% of the cases) comprised tumours beginning in a bronchus and infiltrating lung tissue only. This type would be amenable to treatment in many cases, and during the next few years, radium or X-rays would in all probability be the method of choice. The third type occurred in 25% of the cases and consisted of tumours infiltrating the mediastinum, but not the lung. These growths were formerly considered to be primarily mediastinal in origin, infiltrating the hilum of the lung, but in every case, the main bronchus on one side was found to be involved and the pericardium and great vessels were implicated early. This involvement of vital structures placed it outside the scope of surgery, though possibly it would be inside the scope of radium. The fourth type consisted of tumours infiltrating both lung and mediastinum and would naturally be the most difficult to treat. It comprised the largest group, consisting of the remaining 49% of the cases. He had no suggestions to offer as to how to attack it.

In the first type of carcinoma, intrabronchial radium might be useful as well as bronchoscopic removal of the growth; lobectomy might also be successful. In the second type, lobectomy and possibly radium, were indicated. He could not say much as to treatment in the other two types.

He had recently seen several cases in which X-ray treatment had caused the growth to metastasize more rapidly than would probably have been the case otherwise, and he did not think that X-rays should be regarded as of universal benefit for primary carcinomata in this region. He did not think that X-ray therapy prolonged life in the majority of cases.

He had been interested to hear more than one speaker mention that the sputum was free from tubercle bacilli, a fact which was apparently considered to favour a diagnosis of growth. He, however, considered that the presence of tubercle bacilli in the sputum was not conclusive evidence that the condition in question was not growth; in 5% to 10% of cases of primary intrathoracic malignant disease, tubercle bacilli were present in the sputum. Therefore the investigation of cases must be quite complete, and in suspicious cases, must be carried through even if some other disease in the lung or chest had been discovered.

Section of Surgery.

SUB-SECTION OF PROCTOLOGY.

President—CECIL ROWNTREE, F.R.C.S.

[*December* 11, 1929.]

DISCUSSION ON THE COMPLICATIONS OF OPERATIONS FOR PILES.

PRESIDENT'S ADDRESS.

By CECIL ROWNTREE, F.R.C.S.

RECOLLECTION of the earlier years of my surgical practice, and particularly of the difficulties I experienced, and still experience, in dealing with cases which are not progressing quite as happily as one might wish, led me to select as the subject for our discussion the complications of operations for piles. It might be said that an operation for piles is such a simple matter that when performed on an otherwise healthy patient by a competent operator it should have no complications. But our patients are not always otherwise healthy, as we sometimes find to our cost, nor are all of us competent all the time; and in point of fact, operations for piles are followed by complications of some sort or another often enough to provide all of us with occasional experiences of some of the pitfalls of rectal surgery. If we are lucky enough to escape them in our own work, we are pretty certain to be asked for advice and help in cases arising in the practices of those less fortunate.

The truth is that operations for piles are attended by such a trivial risk to life that they are often lightly undertaken under bad conditions of preparation, anæsthesia, and assistance, by those not really competent to perform them, and still less competent to carry the case to a successful conclusion in the event of some unusual difficulty. The easier and the safer an operation, the greater the discredit if anything goes wrong. It behoves us therefore who claim—or rather aspire to—a wider knowledge of proctology than those who do not belong to this Sub-Section, to see to it that we are fully alive to the possibilities of trouble, even in straightforward cases. When we are dealing with patients who are aged and infirm, or diabetic, or paralysed, or with doubtful hearts, so much the more reason for meticulous care that preparation, anæsthesia, light, operating table, and so on, shall be beyond criticism, for operations upon even such patients as these are possible and safe in the hands of those who have been well and truly trained.

I would like briefly to refer to some of the difficulties I have met with, in the hope that I may evoke a discussion upon debatable points. On some of these there is still considerable difference of opinion expressed in recent text-books, particularly in those of a general nature, that is to say, those from which the ordinary student gets his information. We must try and put this right.

I think the simplest plan would be to take the clock as my guide, and to mention the difficulties I have met with in the order in which they are likely to arise.

Anæsthetics.—Chronologically therefore, we must first turn to the question of anæsthesia, and I may say at once that I have no intention of discussing the relative merits of different methods of anæsthesia in rectal cases, for that subject was adequately dealt with at a recent meeting of the Section of Anæsthetics.[1] We have not, however, always the advantage of the services of a member of that Section, and in the absence of such skilled assistance it is worth bearing in mind that the position of the surgeon prevents him from keeping that watchful half-an-eye on the thoracic end of the patient that is sometimes desirable, and that sudden and complete relaxation of the anal sphincter is an indication that more than half-an-eye is needed at the other end.

[1] *Proc. Roy. Soc. Med.*, 1930, xxiii, 419 (Sect. Anæsth., 11).

Post-operative Pain.—We are often called upon to treat post-operative pain. I must confess here I am all at sea, for while some of my patients have little or none, others have severe pain and I cannot account for it.

We are all agreed that a clumsy, heavy-handed operation induces more pain than one carried out gently and carefully; but, though I try not to be clumsy, there is still pain. Mr. Lockart-Mummery in his valuable book, lays stress upon the importance of maintaining asepsis in pile operations, and claims that by so doing he gets pain-free results, owing to the absence of infection. I follow his technique so far as asepsis is concerned, and I expect we all do, but I do not thereby abolish pain and I do not expect to, for the pain comes in the first twenty-four hours, and it is difficult to believe that infection can have obtained such a hold in that short time as to cause a degree of pain greater than that produced by even grossly infected wounds in other parts of the body.

I have good reason to believe that many skilled and careful surgeons are less fortunate than Mr. Lockhart-Mummery, and that some of their patients, like my own, do get severe pain, and I wonder why.

No doubt post-operative pain depends to some extent upon the choice of operative method. There is, for instance, a general consensus of opinion that the cautery operation is less painful than the various types of ligature operation. On this point I am in a poor position to offer any opinion, for although I was nurtured on the clamp and cautery method, I was soon weaned to the ligature, and since then I have used no other. In my own experience with the ligature method, I have gained a strong impression that pain is less severe in women than in men, and less severe in the aged and feeble than in those more robust and muscular. I am of course speaking of ordinary patients and leaving out of consideration those whose race or temperament renders it impossible to estimate the real degree of pain experienced. Is it possible that well-developed pelvic muscles are an important factor in the pain, and is the pain really due to a reflex spasm of the levatores ani? If it is due to reflex spasm, what induces it? As it appears to follow every type of operation, it must be dependent upon minor details of technique, and I wish I knew what they were.

I expect we are all agreed upon the necessity of avoiding the inclusion of the highly sensitive nerve-endings of the anal margin in the clamp or ligature. But what else can we do towards preventing pain, in addition to taking meticulous care in the details of the operation? Should the sphincter ani be stretched? I notice some difference of opinion on this point. My own impression is that stretching really helps, but I also feel that, unless it is done most gently, the tissues may be damaged so much as to vitiate any benefit that the procedure might otherwise confer.

The utmost care having failed to prevent post-operative pain, what is the best way of dealing with it? In my view there is only one drug that is really efficacious, and that is morphia, and I invariably use it. I know that the present tendency is to regard morphia with some suspicion, and to withhold it if something else can be found to take its place even partly. You will see this reflected in many directions, particularly with regard to dosage. I am convinced that the doses in common use are frequently inadequate, and to my mind to dole out a sixth of a grain to a man weighing twelve stone and in serious pain, is to repeat the torments of Tantalus. I understand from my physiological friends that dogs have a better time in this respect than humans, and that when they are morphinized the dosage is based upon the bodyweight. I came across an interesting paragraph on the subject of morphia in a recent book entitled "Gallipoli Memories," by Compton Mackenzie. It appears that when in acute pain he had had a hypodermic injection of water administered by an optimistic doctor, and he then expresses himself somewhat forcibly as follows:—

"Much has been written of the joys of morphia, and I have to suppose that it gives positive pleasure to many. In my case it performs none of those miracles of pleasure which

are attributed to its magic potency, save only one, and that is its sure paralysis of the most atrocious pain. . . . . If I were set in a position to judge a fellow-man, and that man pleaded addiction to morphia as an excuse for his crime, I would double his sentence, because I should remember the many sufferers who have been denied alleviation of their sufferings through the feebleness of brutes like him."

I suspect that every patient who has had severe pain after an operation for piles, and who has been inadequately morphinized, will subscribe to these sentiments.

Hæmorrhage.—The next complication on my list is hæmorrhage, certainly the most dramatic—and perhaps the most important—complication of an operation for piles, for it is practically the only one that may cost the patient his life.

I suppose it never ought to occur, but none the less it does, and published figures will give you the percentage of its occurrence in the best clinics, with operations carried out in the most favourable circumstances. Both recurrent and secondary hæmorrhage appear to follow every method of operating, with varying frequency. It is true that the percentages are very small, but can we do anything to make them smaller? I think we can, but only by constant attention to minutest details. We ought to try to avoid bad anæsthesia, with incomplete visualization of the operation field; we ought to avoid ligature material that has been boiled once too often; we ought to avoid hurry. I personally once had a hæmorrhage because I was tempted to cut off the pile masses after they had been ligatured, with the result that the ligature slipped. Of course when a patient coughs or strains the tension upon the pedicle of a pile is very great, and it is easy to understand that when the strangulated mass has been much reduced in size it may be pulled up through the loop of the ligature. However careful we may be, it is probable that each of us will at least once in his life have a serious hæmorrhage to deal with. Those who have not yet had a case will be astonished at the quantity of blood that can be poured into the rectum without any external indication at all. I believe that primary—or rather, recurrent—hæmorrhage should always be dealt with by finding and tying the bleeding point, and for this are necessary good anæsthesia, good exposure, and a number of sponge forceps with which to grasp the suspected portions of the soft, yielding and blood-stained tissues without damaging them. The special advantage of sponge forceps is that one can put on several pairs as a temporary measure until one is sure of one's ground.

Secondary hæmorrhage is more troublesome and more difficult to deal with. It is pretty clear that it is due to sepsis, and it is extraordinary to me that it does not happen with greater frequency, for one would expect that the conditions for its occurrence were highly favourable. It seems to be agreed that in cases of secondary hæmorrhage the difficulties of finding and securing the bleeding point in what may be a sloughing area are so great that the best results are obtained by plugging or packing the rectum.

In rectal operations, as in all else, troubles never seem to come singly, and it is noteworthy that if one complication is met with after operation it is very likely that others may declare themselves at a later date; for instance, in cases of secondary hæmorrhage it is quite usual to find afterwards that a stricture has formed, which is easy to understand when one remembers that the underlying basis of both is probably some degree of sepsis in the operation area.

Urinary Complications.—Almost every text-book states that retention of urine should not occur after a properly performed operation for piles, yet every book gives a large variety of alternative methods of prevention and treatment. Some implicate the ligature operation; another says it is more common after the clamp and cautery; again, it is said to be due to stretching of the anal sphincter, or to interference with the anterior wall of the rectum. No doubt it sometimes follows every type of operation, and it would be a very happy thing if we could arrive at some conclusion as to how this complication might be avoided.

My own feeling is that it is in part at least the fault of the surgeon and that trauma is an important factor. I say this because I find it more common in vigorous and muscular young adults, in whose case the operation is more difficult, and I also find that I get fewer examples as I get more experienced. But I still meet with it from time to time, and no one has yet been able to give me a convincing reason as to why it should occur. Of course we are all familiar with the treatment, and no doubt we all go through the whole gamut of letting the patient sit or stand up, putting fomentations on the hypogastrium, inserting belladonna my suppositories, and finally passing a catheter. The whole point in treatment to mind is not to leave the catheter in too long, for if the bladder is allowed to become seriously over-distended then one catherization proves insufficient, and it may have to be repeated for several days. I find this especially the case in women, although, fortunately, post-operative retention is very much less common in the female than in the male.

Miscellaneous.— The next group I want to mention is a rather miscellaneous set of complications that may declare themselves from the fourth or fifth day onwards. Some of them, such as incomplete strangulation of the pile, or prominent tags of peri-anal skin that have escaped excision, are obvious, but annoying, little things, about the treatment of which there is no difference of opinion.

Fissure in ano is another trouble that sometimes appears to develop during convalescence, but I strongly suspect that in most cases the fissure was there before the operation, tucked away between two piles and overlooked. If I am right, this is merely another argument in favour of the great importance of good light and good exposure.

The rarity of the occurrence of abscess and fistula after pile operations affords the best possible testimonial to the care and skill with which we all perform them. I wonder whether the incidence of abscess is greater in cases of strangulated and sloughing piles, and I wonder how far we are justified in operating upon cases of this nature. I know that many think it is better to wait until these things have settled down, but the settling down is a tedious and painful process, and I personally have always preferred to do an immediate operation rather than subject the patient to a trying period of preparatory treatment. Certain safeguards are necessary ; for instance, it is important to remember that the peri-anal tissues are œdematous and swollen, and that it is easy to remove far too much. The method selected is important, and I invariably use the ligature method by the single tie, and avoid transfixion of the swollen mass, for I think that transfixion or dissection of these tissues—already possibly infected—is taking a risk, small though it may be.

Stricture.—The patient who exchanges his piles for a stricture is reminded every day of his life of the bad bargain he has made, and no doubt he thinks—and possibly speaks—each day, of the surgeon who effected the exchange. Of course, there are strictures *and* strictures—those which are met with in our own practice we call constriction bands—a term which has a less guilty sound than stricture. I wonder how far we are guilty, and how far these strictures are preventable? Do they turn upon errors of operative technique, or errors in the after-treatment, or is it the patient's fault? It seems pretty clear that they do happen from time to time in cases operated upon under the best conditions—how often it is difficult to say. Some figures will put it as high as 5%, and, of course, I leave out of account Whitehead's operation, which I suppose is now very rarely done.

What is the pathology of stricture? If, as I suppose, it is due to fibrosis and contraction of granulation tissue in the submucous layers, it can only be caused either by trauma or by infection, and in considering this point, I wonder whether there is any agreement as to the relative frequency of contraction according to the type of operation employed. It is agreed, I think, that it is less common

after the clamp-and-cautery operation, but as I take it that some form of ligature operation is the one that the vast majority of us employ, it is interesting to speculate as to whether there is any difference in the frequency of contraction according to the exact type of ligature operation employed. It is not quite right I think to lump all ligature operations together under one heading, for in my view they resolve themselves into two distinct classes. Firstly, the type in which the whole pile is ligatured *en masse* without any dissection or transfixion or cutting beyond the V-shaped incision of the peri-anal skin, which is so necessary in order to avoid its inclusion in the ligature. The second type of operation is one in which an attempt is made to strip up the pile from the rectal wall until a definite pedicle is made, which is then transfixed and ligatured. It is clear that in the first method there is little or no interference with the submucous tissues, while by the second method a raw surface is left which must, in any case, granulate, and which is obviously exposed to infection.

It is my definite impression that contraction bands are more common after the second method of operating than after the first, but of course it is not easy to be emphatic on points like these because I suppose most of us are more or less committed to a particular type of operation, and few of us have the opportunity of personally carrying out experiments in technique on a large enough scale to give us convincing evidence.

Mr. ASLETT BALDWIN said: I have not seen any serious complication in any of my own cases. The main factor in their prevention is the avoidance of sepsis. I perform the operation without stripping up or dilatation of the sphincter. I first swab thebowel out as high up as possible with perchloride of mercury lotion and after operation insert the two index fingers and gently dilate the mucous membrane, if there is any tendency to constriction. I then dust in an antiseptic and anæsthetic powder, such as boro-chloretone. If the patient is very nervous I inject urea and quinine solution all round. If skin tags have been removed, lano-cyllin ointment with anæsthesin is applied. Solid food in moderate quantity, and paraffin by mouth are given as soon as possible, and 2 or 3 oz. of warm olive oil are injected into the bowel and left there as soon as the first aperient is given; this prevents pain when the bowels act.

Mr. E. T. C. MILLIGAN: Stricture of the anal canal, or "constriction ring" as it is called, is a complication of piles which one feels should be avoided. Its formation is identical with inflammatory strictures in all tubes of the body. Inflammatory products at the site of injured surfaces stiffen and set the tissues in their usual closed position. Later these inflammatory products are replaced by fibrous tissue, and so an inelastic ring is formed which does not dilate with the rest of the canal during the passage of its contents.

The site of the constriction ring is the upper third of the anal canal (fig. 1). It can be seen through the proctoscope and detected by the examining finger at that site, the twelfth day after operation (fig. 2).

Statistics of the occurrence of this type of stricture are as follows: In a series of 282 operations for piles, it occurred in 32 cases = 11·3%. In a series of 290 operations for piles it occurred in 27 cases, = 9·31%. The types of operation performed in the above series were those known as the clamp-and-cautery, and ligature following the stripping up of the pile.

It is easy to see why stricture formation must follow when, after cutting into the submucous layer at the skin base of the pile, the pile is stripped along this layer off the muscles and a ligature is placed round its pedicle at the upper third of the anal canal, a narrow part of the anal canal where sphincter action is tightest, for a large bare area corresponding to the amount and thoroughness of stripping and high ligation of the pedicle of the pile is left in the anal canal (fig. 3). When three or more large piles are thus removed and the ligatures subsequently separate, a large bare ulcerating area encircles the upper third of the anal canal and stricture is likely to result.

In the clamp-and-cautery and in the suture methods of pile removal the mechanism of production is essentially the same, for, although the lines of crushed or sutured mucous membrane corresponding to the removed piles are adherent at the end of the operation, they subsequently separate and become bare areas healing by second intention.

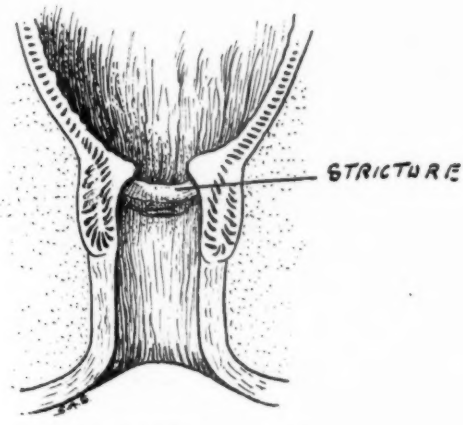


FIG. 1.—Site of stricture in anal canal.

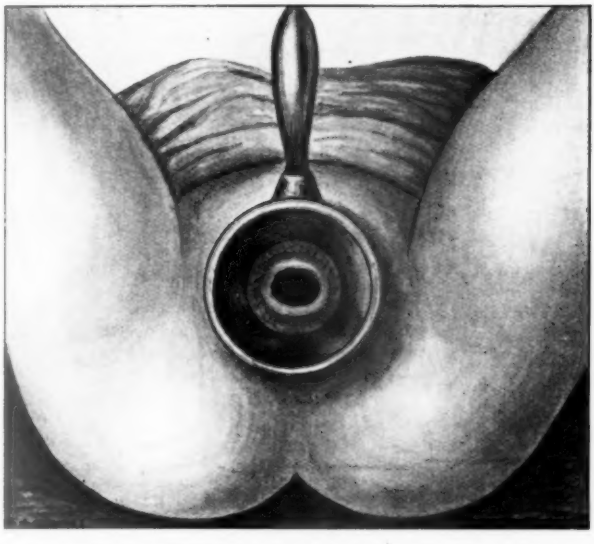


FIG. 2.—Stricture of anal canal seen through proctoscope.

To prevent constriction rings it is suggested in text-books that the ligatures should be applied at different levels, which implies varying degrees of "stripping up," so that subsequent fibrous tissue will not wholly encircle the lumen; for it is only when fibrous tissue surrounds the whole tube that harmful stricture results (fig. 4). To carry this out is difficult and unsatisfactory. A method of removing piles which theoretically should never be followed by stricture, and which indeed in a large series of cases over many years closely observed for

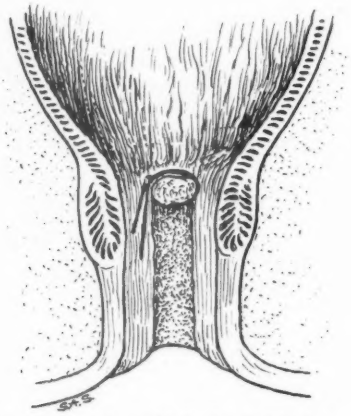


FIG. 3.—Bare area in anal canal following "stripping up" of pile.

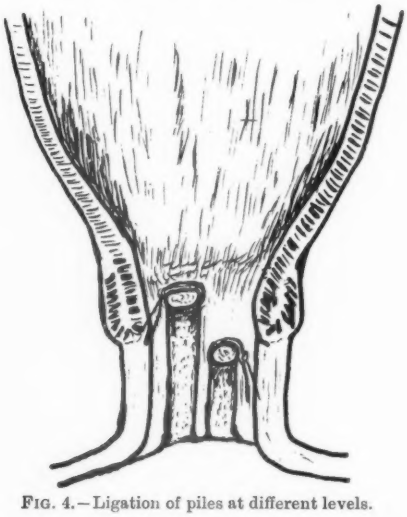


FIG. 4.—Ligation of piles at different levels.

this point, has never been followed by constriction ring, is one which, firstly, does not strip the pile off the wall of the anal canal; and secondly, leaves comparatively large areas of intervening intact healthy skin and mucous membrane between the ligated hæmorrhoids (fig. 5) in striking contrast to the "stripping up" operation (fig. 6). The technique recommended is as follows: A V- or U-shaped incision is made only through the skin at the skin base of the pile or if necessary at the base of the associated skin tag (fig. 7). In this groove the ligature is laid

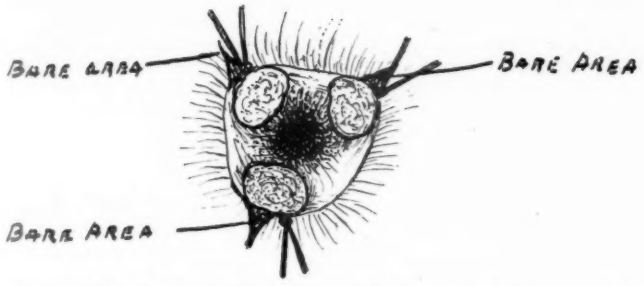


FIG. 5.—Three radiating incisions representing the only bare area. Large areas of intervening intact healthy skin and mucous membrane between ligated hæmorrhoids.

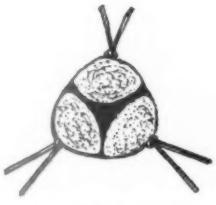


FIG. 6.

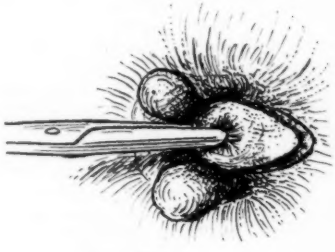


FIG. 7.

FIG. 6.—"Stripping up" operation completed. Constriction of anal canal by ligatures. Inadequate areas of normal mucous membrane between ligatures.

FIG. 7.—Incision at skin base of pile.

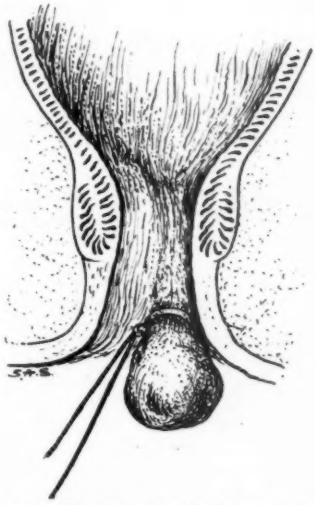


FIG. 8.—Ligation of "pulled down" pile.

and the pile pulled down over the ligature, which is then firmly tied high up in the anal canal and left strangling the pile—thus the mucous membrane of the upper part of the anal canal is tied down to the lower part in segments of the anal canal corresponding to the piles removed instead of being "stripped up" (fig. 8). Till the ligatures separate, three radiating incisions at the anus represent the only bare areas (fig. 5). When the ligatures separate, the dragged-down ligated mucous membrane of the upper end of the pile has already become adherent and so does not retract.

For completeness it may be mentioned that constriction rings are easily managed by weekly dilatations with finger or with bougie, and that full dilatation and elasticity are effected in from three weeks in most cases, to some months in others. It is, however, an unpleasant and sometimes painful proceeding for the patient.

If constriction ring does not occur during convalescence it will not appear subsequently.

It is only in the cases not detected, and therefore untreated, that symptoms of difficult defæcation arise.

If the "stripping up" operation were abandoned then there would be no anxiety about post-operative stricture of the anal canal.

Mr. CECIL A. JOLL said that with regard to Mr. Milligan's statement that in his operation for piles he left a broad area of mucous membrane between the piles which he had ligatured, his (Mr. Joll's) experience was that when primary piles were large, especially when associated, as they often were in these circumstances, with secondary piles, it was quite impossible to succeed in leaving this broad intervening band of mucous membrane.

If one measured the total amount of membrane involved by primary and secondary piles, the percentage of normal membrane left was often small.

Mr. TURNER WARWICK said that, although he agreed with Mr. Milligan that the high ligature was usually responsible for the constriction ring, he could not agree as to the mechanism of its formation. The surgeon often produced extreme narrowing of the lumen at the time of operation, by firmly drawing down the pile, and then, after some dissection, gathering within the compass of a very tightly-tied ligature the mucosa and submucosa from an area which seemed small when the pile was being firmly dragged down by an assistant. This area, when released from all tension, was extensive and roughly triangular in shape. Only too often the extremities of the base of such a triangle were points widely separated on the circumference of the anus, and the apex a point far higher above the base than was necessary.

When the surgeon had tied such a ligature and had released the pedicle, the pull on the mucosa—greatest above the apex—everted the mass into the lumen. The constriction resulted from the organization of the diaphragm formed by three or more of these everted masses.

He thought Mr. Milligan's diagrams illustrated this very clearly. Tearing down the diaphragm at the time of operation often failed to prevent the constriction ring. This procedure merely produced linear tears in the taut mucous membrane, and the diaphragm tended to re-form and organize as these tears healed.

The bare area itself usually healed and epithelialized readily and its presence played little direct part in the formation of the constriction ring above it. The formation of a constriction ring could only be effectively prevented by minimizing the "bunching" produced at the time of operation.

Mr. W. B. GABRIEL: Of all the complications of operations for piles I believe the most serious is post-operative ulceration with stricture formation. Once this condition develops, the after-treatment may need to be continued for months or years, and a rectum so affected will probably never return to a normal condition. In preventing this condition the following two points are of great importance:—

(1) Operation should never be performed on septic piles. If an internal pile is prolapsed and thrombosed, sloughing or ulcerated, it should be treated on expectant lines. The patient should be confined to bed and antiseptic compresses should be applied at 4-hourly intervals. I prefer 1 in 2,000 perchloride of mercury for this purpose. Under this treatment most infected piles will undergo spontaneous cure: the sloughs will separate, leaving clear, granulating areas, thrombosed piles will organize, and if later any other piles appear prominent I think it is better to treat them by high carbolic injections.

(2) The technique of the operation for internal piles presents many points on which I should like to give a dogmatic opinion.

(*a*) The Whitehead operation should never be performed.

(*b*) I have abandoned the clamp-and-cautery operation: it is liable to cause unpleasant external œdema; I have seen severe post-operative ulceration afterwards.

(*c*) The ligature operation is the method of choice.

For the last year I have used local anæsthesia in almost all cases: full relaxation of the sphincter can be obtained, and the absence of post-anæsthetic vomiting is a great help in obtaining a neat end-result.

At operation, one point is of paramount importance—the piles should not be stripped up high. When they are held in artery forceps, with the sphincter relaxed, the ligature should be applied at the level of the anus and no higher. High stripping leads to extensive denudation of the lower rectum, a variable amount of ulceration is then inevitable and a long after-treatment is needed. My practice is to use No. 2 chromic catgut for the ligature material, and I invariably transfix each pile with a curved round-bodied needle, the ligatures being cut short. I am convinced that this technique is superior to ligature with silk, when the ends of the ligatures are left sufficiently long to hang out of the anus. These ligatures in a few days present as a dirty mass hanging from the rectum: they are really infected foreign bodies which must produce local irritation and sepsis. I have used catgut for the last nine years, and am certain that with the technique indicated above the healing is far smoother and more rapid than with any other method I know.

Mr. W. S. PERRIN said that for preventing pain in pile operations a preliminary division of the pecten band, as advised by Mr. Ernest Miles, was very effective as it rendered digital dilatation of the anus unnecessary. Digital dilatation forcibly ruptured the pecten band and caused bruising, to which much of post-operative discomfort was due. The old-fashioned, ligature operation in which the piles were dissected up in three masses, leaving three vertical zones of intact mucosa between the denuded areas, was the most satisfactory. Provided sufficient intact mucous membrane was left between the ligatured piles, stricture need not be feared, while ligaturing the piles with stout silk made hæmorrhage impossible. Mitchell's operation, though a very good one, had, in his experience, occasionally been attended by a mild secondary hæmorrhage and occasionally also accompanied by severe post-operative pain, probably from the collection of infected exudate under the continuous catgut stitch. However thorough the attempt to disinfect the anal canal, sterilization could not always be ensured and it was probably wiser to leave a bare area to granulate than to attempt the primary union essential to the success of Mitchell's method.

SPECIMENS SHOWN.

By W. B. GABRIEL, M.S.

I.—Papilliferous Type of Carcinoma of the Rectum. A longitudinal slice through an early cancer of the rectum. The patient, F. L., a woman, aged 64, complained of bleeding and discharge from the rectum, of twelve months' duration. Sigmoidoscopy revealed carcinoma of the rectum and perineal excision was performed. The interest of the specimen lies in the fact that the cancer has spread by direct continuity only as far as the circular muscle coat. The longitudinal muscle is not penetrated in any region and there is no peri-rectal spread. The lymphatic glands do not contain metastases. A few small adenomata were found scattered about the mucous membrane above and below the growth.

II.—Cancer of Rectum associated with Villous Papillomata.—The specimen shows an ulcerating cancer near the recto-sigmoidal junction and a large villous papilloma just above the ano-rectal line, from a man, aged 75, who had suffered from diarrhœa and constipation for several months, and lately from profuse

bleeding. Colostomy was performed followed by perineal excision of the rectum; convalescence was complicated by severe bronchitis. Death from bronchopneumonia. Microscopic examination shows the upper tumour to be an adeno-carcinoma which has spread by direct continuity into the peri-rectal tissues. The lymphatic glands contain metastases. The villous tumour immediately above the ano-rectal line shows no sign of malignant change.

III.—Lymphoma removed by Local Excision from Wall of Rectum.—The patient, S. W., a man, aged 32, had a polypoid tumour of the lower part of the rectum; it was removed and the tumour considered clinically to be a fibroid polyp: microscopic examination shows the tumour to be a lymphoma. The mucous membrane is intact except for a small ulcer over the summit of the tumour; there is no proliferation of the epithelium or connective tissue; the tumour consists of aggregations of lymphoid cells situated in the sub-mucosa and muscle coat.

IV.—Omentum containing Metastases from Cancer of Rectum.—The specimen shows a portion of the omentum removed at laparotomy. It contains two large metastases from a colloid cancer of the rectum, from a man, aged 30.

By LIONEL E. C. NORBURY, F.R.C.S.

I.—Rectal Carcinoma, treated by Radium and Subsequent Excision.—Mrs. S., aged 48. Admitted August, 8, 1929.

On Examination.—Malignant ulcer, with raised edges, on anterior wall of middle third of rectum, adherent to vagina. *Treatment.*—Radium needles inserted *per vaginam*, 1 cm. apart—15 needles, 40 mgm., 5,920 mgm. hours. *Re-admitted* November 9, 1929: Growth had increased in size. November 13, 1929: Laparotomy No metastases in glands or liver. Left inguinal colostomy. November 23, 1929: Perineal excision of rectum together with portion of posterior vaginal wall.

Description of Specimen.—The total length of the specimen was 5 in. An ulcerating growth 1½ in. in longitudinal axis and 2½ in. in transverse axis, was situated on the anterior wall of the rectum; the lower margin of the growth was ½ in. above the ano-rectal line, and there was 2 in. free margin above the tumour which was entirely infra-peritoneal.

Running through the ulcer in the mid-line anterior is a broad scarred band about ½ in. in width with a branch running upwards and to the right.

The tumour is an adeno-carcinoma which has spread by direct continuity into the peri-rectal tissues. The ano-rectal lymphatic glands do not contain any metastases. The broad band running up the middle of the ulcer is scar tissue and marks the site of the most extensive radiation. The fibrous tissue extends from the anterior wall of the rectum to the vagina and includes a few degenerating cancer cells. The surface of the scar is not covered with epithelium, and there does not appear to be any regeneration of epithelium.

II.—Meckel's Diverticulum, showing Metastases from Carcinoma of Pelvic Colon.—H. W., male, aged 62.

History.—Eight months; bowels opened four to six times daily; no bleeding or discharge; some loss of weight. *Digital Examination of Rectum.*—Tumour just palpable. *Sigmoidoscopy.*—At 13 cm., typical carcinomatous ulceration; fragment removed for microscopic examination. Report: Adeno-carcinoma. *Operation.*—Large carcinoma of pelvic colon fixed to left wall of pelvis; glands in front of sacrum; (?) deposit in liver. Meckel's diverticulum present with hard nodule in it; diverticulum removed; left inguinal colostomy performed.

Microscopical Report on Meckel's Diverticulum.—At the distal end, the mucous membrane is ulcerated and the submucosa and muscle coat infiltrated with a deposit of adeno-carcinoma. The diverticulum had been invaded by the carcinoma cells from its outer coat inwards, as shown by the fact that the carcinomatous mass has approximately a triangular shape, the base being situated on the serous coat and the apex in the mucosa.

By H. J. B. FRY, M.D.

I.—Carcinoma of the Rectum with Diverticulosis.—A. B., male, aged 55. Had suffered from constipation all his life, with increasing difficulty during last three months: had recently passed a little blood. A rectal growth was removed by abdomino-perineal excision from the upper rectum. It showed deep excavation, and above it in the pelvic colon were numerous diverticula, which, in the fresh state, were filled with rounded fæcal concretions: below the growth a few sessile papillomata could be seen. Microscopically: A columnar-celled carcinoma infiltrating the muscularis mucosæ and reaching, but not penetrating, the circular muscular layer: in places the growth shows slight colloid degenerative changes. Lymph gland shows no invasion by growth.

II.—Colloid Carcinoma of the Rectum with secondary deposits in the Skull.—R. B., female, aged 20. Admitted March 13, 1926, under Mr. Rowntree, with an ulcerating cauliflower growth on the posterior wall of the rectum, involving about one-third of the wall. Laparotomy revealed a large mass of hard glands in the pelvis. Colostomy performed.

April 12, 1926.—Radium needles were inserted, 52 mgm. for twenty-four hours. Re-admitted November 12, 1926: Growth completely surrounding lumen of rectum and nodule in vaginal wall. Irradiated 42·5 mgm. radium for forty-eight hours. Re-admitted April 16, 1927, with intense pain in back and down left leg: general condition bad: pain at external angle of right orbit and paralysis of right external rectus with diplopia. Severe cystitis present: headaches: semi-conscious.

Post-mortem Examination.—June 1, 1927: Carcinoma recti. Metastases and double pyonephrosis. Skull showed flattened nodules of growth on the surface beneath the scalp. On inner surface of skull there were about twenty nodules of growth of varying size: base of skull showed nodules of growth in anterior and middle fossæ and surrounding pituitary body involving cavernous sinuses: brain itself free from growth: peritoneum showed nodules scattered on the surface: pelvis almost obliterated by growth and all the pelvic organs were invaded: high degree of cystitis. Rectum and perirectal tissues were a mass of growth which had invaded the walls of the pelvis: abdominal glands invaded and liver extensively infiltrated: small nodule in right lung and cervical glands enlarged.

III.—Large Papilloma (? Carcinoma) of the Rectum.—E. H., male, aged 57. Admitted January 16, 1929, complaining of rectal hæmorrhage for one year and increasing constipation: had previously had a colostomy (November, 1928). Perineal excision was performed.

Naked-eye Condition.—On posterior wall of rectum a large papillomatous mass with a short broad pedicle, with no evidence of invasion of the rectal wall: microscopy.

Microscopically.—A papilloma in places undergoing colloid degeneration. The pedicle shows chronic inflammatory infiltration and some apparent invasion. No definite evidence of invasion of the submucous layer of the rectum.

By E. ADAMS CLARK, M.B., B.S. (for A. LAWRENCE ABEL, M.S.).

Double Carcinoma of Pelvic Colon and Rectum associated with Polyposis of Colon and Duodenum.—Patient, male, aged 63. Admitted to Passmore Edwards Cottage Hospital, September, 1929, with four months' history of frequent attacks of diarrhœa accompanied by aching pains in lower abdomen. Each attack lasted ten days with only from two to seven days' freedom. No blood or mucus in stools but some loss of both appetite and weight: on rectal examination a large growth was felt at the pelvi-rectal junction: an exploratory laparotomy was

performed and a large growth of border-line operability was found. In view of the patient's general condition, only a colostomy was performed and patient was transferred to the Cancer Hospital for further treatment: unfortunately shortly after admission symptoms of pelvic abscess developed and rapidly proved fatal.

Post-mortem Examination.—Two separate carcinomata were found, one at the pelvi-rectal junction (3 cm. by 2·5 cm.) and one larger (5 cm. by 5·5 cm.), 1·5 cm. higher up, the two being separated by healthy mucous membrane.

Throughout the extent of the colon, multiple polypi were present, in increased number in distal portion of large intestine; three distinct papillomata were also present in the duodenum just beyond the pylorus.

The case is of interest for the following reasons: (1) It is an example of double carcinoma of the large intestine; a condition itself somewhat uncommon; (2) the double carcinoma was associated with multiple polypi in the colon and in the duodenum.

Multiple intestinal polypi are rarely found. In a series of 17,000 autopsies, Stœmmlev of Chemnitz found polypi in only 0·7%, and of these, in only one case in twenty were the polypi multiple.

The association of carcinoma with multiple polypi is common; in a series of cases of carcinoma of colon and rectum, reported by C. E. Dukes, simple tumours were present near the carcinoma in twenty-five out of thirty-three instances.

By CECIL A. JOLL, M.S.

I.—Uterus, Appendages, and Rectum: Squamous Epithelioma.—This was removed by a combination of Wertheim's hysterectomy and abdomino-perineal excision of the rectum on October 15, 1926, from a patient aged 43, who had had a watery blood-stained discharge from the vagina for six months. The specimen shows a large fungating growth of the posterior vaginal wall. It extends from a point half an inch above the vulva to the posterior lip of the cervix, and is two inches across at its greatest width. The rectal wall is involved as far as the submucous layer. A large infiltrated gland is displayed at the extreme right of the specimen near its upper end. Microscopically the tumour had the structure of a squamous epithelioma.

The patient left the hospital with the wound healed within three months.

II.—Endometrioma of Rectum.—This specimen was removed on August 14, 1928, by abdomino-perineal excision, a longitudinal strip of the rectal wall only is preserved. The patient, a woman aged 34, whose chief symptom was hæmorrhage from the rectum, was found to have a tumour of the rectal wall and was admitted to the Cancer Hospital for operation. The tumour is outside the mucous membrane of the rectal wall, though involving the muscular coats. It is a typical endometrioma.

Patient was well on January 1, 1930.

Section of Otology.

[*December* 6, 1929.]

SUBJECTS FOR DISCUSSION: THE DIAGNOSTIC VALUE OF X-RAY EXAMINATION OF THE TEMPORAL BONE, AND THE DIAGNOSIS OF EIGHTH-NERVE TUMOURS.

Radiography of the Mastoid Process.

By Elsie Mann, M.B., D.M.R.E.

The X-ray examination of a patient for disease of the mastoid process can be divided into (1) the taking of the photograph and (2) the interpretation of what the photograph shows. In making X-ray photographs of any part of the body it is advisable to standardize conditions as far as possible. By using the same position of the patient, the same current and the same spark-gap, a more just comparison can be made between films taken from the same patient at different times. The only thing which cannot be standardized is the patient, and so from time to time, modifications may have to be made, but when possible a standard technique should be employed.

Technique.

The technique which I use in making X-ray photographs of the mastoid regions depends on whether or not the patient is old enough to keep still for an appreciable length of time. If it will keep still, then I use a Potter-Bucky diaphragm in making the picture. This is a mechanical device by which a moving grid cuts off scattered radiations and so gives clearer pictures, but which considerably lengthens the time of exposure. One mastoid process is flung clear of the other by tilting the X-ray tube to an angle of 30° with the horizontal, so that the photographic ray enters the skull obliquely from above. The patient is made to lie with the ear to be photographed nearest the film, and the tube is centred just above the opposite ear. The exposure is then made. The patient is turned on his other ear and a second film is exposed in a similar manner. With the X-ray plant which I have at my disposal, the necessary exposure during this technique is a matter of eight seconds. This is a long time for a small child to stay absolutely still, so when the patient is very young I concentrate on making the exposure as short as possible. For this reason I do not use a Potter-Bucky diaphragm when the exposure is cut down to less than a second. Instead of tilting the X-ray tube to get one mastoid region clear of the other, the same result is obtained by resting the child's head on a wooden block which subtends an angle of 30° with the table. This block carries the casette containing the film, and the child rests the ear to be photographed on it as on a pillow. The X-ray tube is centred just above the other ear, and the photographic ray enters the head vertically. The exposure is made, and afterwards the process is repeated for the other ear.

As far as may be, during the whole of the taking, developing and fixing of the films, exactly similar conditions are reproduced for each, so that as nearly as possible the two pictures will be photographically similar. Sometimes with children it is extremely difficult to ensure them staying exactly where they have been placed, but I have never found any clamp of use in helping to keep them still. It has frightened them and negatived its own usefulness by causing them to move.

The right and left positions which I have described are the only ones I now use for taking X-ray photographs of the mastoid processes. For some time I used, in addition, a prone position, with the chin stretched out over—and resting on—the film. The tube was centred over the vertex of the skull. The chief point about this position was that it brought the mastoid processes on one plate and so made comparison easier. This view was occasionally of value, but not so sufficiently often to justify its routine use.

The type of case which presents most difficulty in making X-ray photographs of the mastoid regions is: (1) That of the very young child. I have found that to get a picture which will be of any diagnostic value from a child under 3 years of age is often more a matter of luck than of good management, unless the X-ray plant being used is sufficiently powerful to make the exposure instantaneous. (2) That of the refractory child. Every now and then in an X-ray department there appears for examination a child who is unmanageable. No amount of coaxing or cajoling has any effect, and, after exhausting the patience of everyone round, the child is despatched without being photographed or else a few useless blurred films are the result.

The radiologist's task is not over with the production of successful photographs. The films have to be interpreted. That this is not always easy I hope to demonstrate in the six cases I have chosen for illustration.

Although in the majority of cases the right and left mastoids are similar, it must always be borne in mind that anatomical variations do occur, and that a cellular mastoid may be present in one side and a non-cellular one on the other.

Frederick M. Law makes a statement with regard to mastoids which is often of great use to the radiologist.[1] He says that, with infrequent exceptions, if there is a cellular mastoid on each side, the cells composing these mastoids will be symmetrical. This fact is useful when trying to come to a conclusion as to whether a suspected place in the film is a large cell or the result of bony absorption.

The type of case which is most difficult of diagnosis is that in which both ears are affected. The comparison of right side with left side is then lost to a large extent, and the diagnosis must depend on the appearance which that type of mastoid would ordinarily present.

Illustrative Cases.—T. B. LAYTON, D.S.O., M.S., and ELSIE MANN, M.B.—(I) J. H., girl aged 5. Scarlet fever. Spontaneous right otorrhœa on seventh day of disease. Radiographed six weeks later.

Operation.—Gelatinous granulation tissue in mastoid cells.

Bacteriological Report.—A pure growth of *Staphylococcus albus* obtained. Wound healed and ear dry three weeks afterwards.

Drum-head: no discharge. Small dry perforation in right drum-head.

November 13, 1929.—Small perforation; middle ear dry.

(II) G. W., boy, aged 3. Scarlet fever. Right otorrhœa on nineteenth and left otorrhœa on twenty-first day of disease. Radiographed eight months afterwards. Right ear was dry for one month.

Operation.—Large mastoid cavity. One large cell with gelatinous mucosa.

Bacteriological Report.—Pure growth of *Micrococcus catarrhalis*. Ear dry fifteen days later and wound healing.

On discharge right drum showed large dry perforation; left drum-head apparently intact.

November 13, 1929.—Left drum-head intact; right, large perforation with healed margin—mucous membrane beneath moist.

(III) W. M., boy, aged 3. Scarlet fever. Right otorrhœa, chronic for one year before admission. Radiographed. Permission for operation refused. Left hospital

[1] "Annals of Rœntgenology: A Series of Monographic Atlases." Vol. I. Mastoids, by Frederick M. Law.

with ear discharging and partial destruction of drum-heads. Seen afterwards, ear dry for one month.

November 13, 1929.—Destruction of drum-head on each side; ears dry.

Skiagrams shown by T. B. LAYTON, D.S.O., M.S., and ELSIE MANN, M.B.—G. L., boy, aged 16. Scarlet fever. Left otorrhœa on eleventh day of disease. Retro-aural swelling six weeks later; Wilde's incision. Radiographed a week later. Operation: large cell containing fluid; diseased bone. Bacteriological examination not made. Ear discharge ceased after twenty-five days. Drum-head intact on discharge, but small unhealed sinus present posteriorly.

D. R., girl, aged 5. Scarlet fever. Right otorrhœa on fourth day of disease. Radiographed three months later. Operation: diseased bone and granulations in mastoid cells. Bacteriological examination not made. Ear dry; wound healing three weeks afterwards. On discharge: small dry perforation in right drum-head; child very ill during early stages.

A. A., boy, aged 3. Scarlet fever. Left otorrhœa on seventh day of disease. Radiographed eight weeks later (during this time otorrhœa had twice stopped for short periods).

Operation.—Left antrum apparently healthy.

Bacteriological Report.—"Sterile."

Ear discharge continued for eight more weeks. Drum-head, on discharge, intact.

Illustrative Cases.—T. B. LAYTON, D.S.O., M.S., and J. V. ARMSTRONG, M.B.—(I) G. L., aged 14. Had running-ear before scarlet fever. While in hospital, virulent diphtheria bacillus was found in the discharge from the ear and persisted for many weeks; postero-superior marginal perforation with granulations suggested disease of mastoid. Diagnosis supported by X-ray findings. Mastoid opened; cultivations from bone showed *Streptococcus hæmolyticus* only. Bone-work of radical mastoid performed; cavity filled from temporal muscle, no skin flap made. Diphtheria bacillus disappeared at once from discharge. Wound healed and ear became dry. Seen in September, 1929. Ear discharge recurred. Swab from ear. No diphtheria bacilli found. When shown again, middle-ear quite dry.

(II) R. D., male adult. Scarlet fever. After the temperature due to the disease had subsided it rose again and there was discharge from the ear, with some pain. Skiagrams showed definite difference between the two sides of the mastoid.

Operation.—Pus in mastoid. Considerable disease of bone; lateral sinus very deep and very far forward; antrum and iter not discovered.

Cultivations.—No growth, except, after four days, a few staphylococci, due to contamination.

(III) E. F., girl, aged 5. Scarlet fever. Admitted May 28, 1929, on second day of disease. Temperature did not settle. Vomited June 7; otorrhœa June 11 without pain or alteration of temperature. No further ear symptoms; discharge profuse. Radiographed July 23, 1929.

Operation.—August 7, 1929.—Pus in antrum: diseased bone curetted away.

Discharged September 7, 1929. On discharge: wound healed; perforation with healed edges; middle ear dry. No active disease.

The Diagnostic Value of X-ray Examination of the Temporal Bone.

By H. K. GRAHAM HODGSON, C.V.O., M.B.

IN studying radiograms of the labyrinth in cases of otosclerosis, I have noted that the extent of the bone changes does not seem to have much bearing on the severity or otherwise of the patient's symptoms. There are cases in which the

clinical signs and symptoms are very distinct, and yet the bone changes are only slight. In another case with slight symptoms, the bone changes are very noticeable. One is reminded of arthritis in other parts of the body. The pain seems to depend not on the extent of the bone changes so much as on whether or not they involve the nerves.

In one-third of the cases in which there is clinical doubt I find changes which I have only seen associated with otosclerosis.

In one of the remaining two-thirds I could not detect any X-ray evidence of abnormality. This does not mean that they are normal. It simply means that I have been unable to detect any abnormality radiographically. With the best radiograms possible I do not consider that one could see the earliest changes round the oval window or in the basal cochlea.

The remaining third are cases in which there is some slight lack of definition in the basal portion of the cochlea; in those cases I cannot say whether the condition is pathological or merely a variation from the normal. So that only in about a third of the cases can one by means of X-rays confidently detect the changes due to otosclerosis in the labyrinth.

In the future, when some treatment for the condition has been discovered, radiography may be of use in tracing the progress of bone changes during such treatment. It should also be of use in the selection of cases for treatment, because it is reasonable to suppose that cases with the least bone changes would yield to treatment better than those with marked bone changes. From the diagnostic point of view I do not think it is at present of much use, except in one-third of the cases, therefore I should like to see this work carried on from the research point of view in hospitals, where there are the best opportunities of collaboration with colleagues; one can X-ray the cases as often as one wishes, estimate the degree of change and so on, and even if one is not doing that patient any good, one is gaining experience in an exceedingly difficult and interesting branch of radiology, and it costs the patient nothing.

[Dr. Graham Hodgson then showed other slides illustrating difficulties of diagnosis.]

Two Skiagrams of the Temporal Bone.—E. WATSON-WILLIAMS, M.C., F.R.C.S.Ed.

(1) Skiagram showing extensive destruction of the squamous temporal bone by cholesteatoma. Adult male patient: radical mastoid operation several years previously. Complains of swelling in temporal region, and continuous headache. The skiagram shows that an area of temporal bone, about 3 cm. in diameter, has been entirely destroyed by what was found at operation to be a cholesteatomatous mass exactly resembling in colour, size and shape a ping-pong ball. Complete recovery.

(2) Skiagram showing infection of mastoid cells in acute otitis media. The question arose whether a mastoid operation was necessary, and the skiagram would indicate that it was. No operation; complete recovery. Second skiagram a month later, showing normal mastoid cells.

Osteomyelitis of the Temporal Bone.—W. A. MILL, F.R.C.S.—F. H., male, aged 50. Admitted to Guy's Hospital with acute mastoiditis August 8, 1929, after 6 weeks' otorrhœa. Schwartze operation performed. Discharged August 17, 1929. On September 19, 1929, the drum-head and wound were healed, but for a week there had been a swelling in the temporal region. This persisted, and the patient complained of headache and pain.

X-ray examination October 14, 1929, showed "rarefaction indicative of infection of the squamous portion of the temporal bone" (fig. 1).

October 19, 1929.—The ear was discharging, and there were granulations in the middle ear. Swelling was most marked above the zygoma, but extended over the whole area of the temporal bone.

Mastoid reopened. Granulations in cavity. Radical operation. Malleus and incus covered with granulations.

Large scalp flap turned down and diseased bone removed (fig. 2). The outer table was reddened and very soft. A layer of granulation tissue extended between the two tables. Over the whole area the dura was thickened and whiter than normal. Anteriorly near the great wing of the sphenoid there were a few granulations on it.

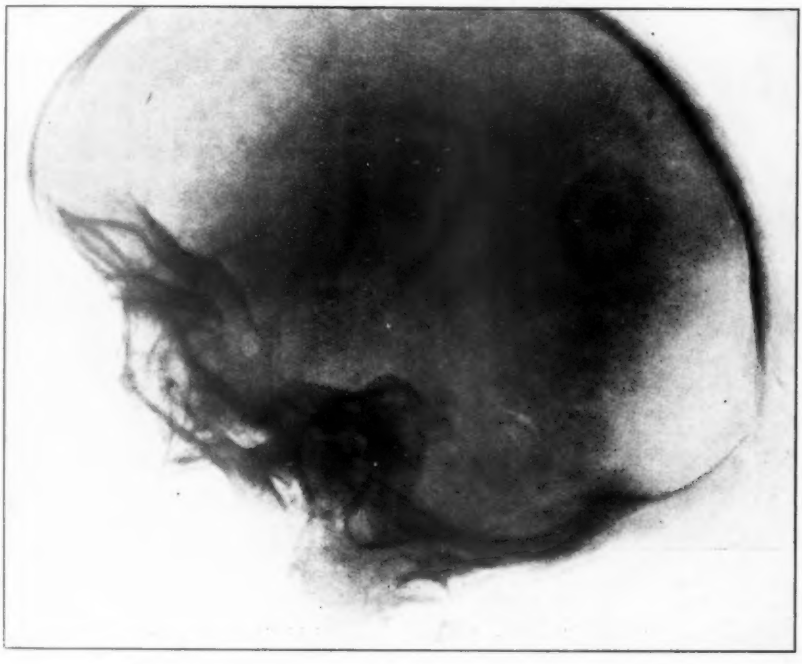


FIG. 1.

Flap replaced and sewn in position. Mastoid wound left open. Drainage through lower end of flap incision.

November 18, 1929.—Not quite healed, but patient would stay in hospital no longer. Fig. 2 shows that further small sequestra are separating.

POSTSCRIPT.—There is now (December 16, 1929) some thickening over the region of the masto-occipital suture, and further X-ray examination (November 30, 1929) indicates that there is rarefaction, but it is possible that this may be evidence of healing and not infection. The intention is to watch the case and, if necessary, take further skiagrams. The organism found at the time of the original mastoid operation was a Gram-positive coccus, probably a streptococcus.

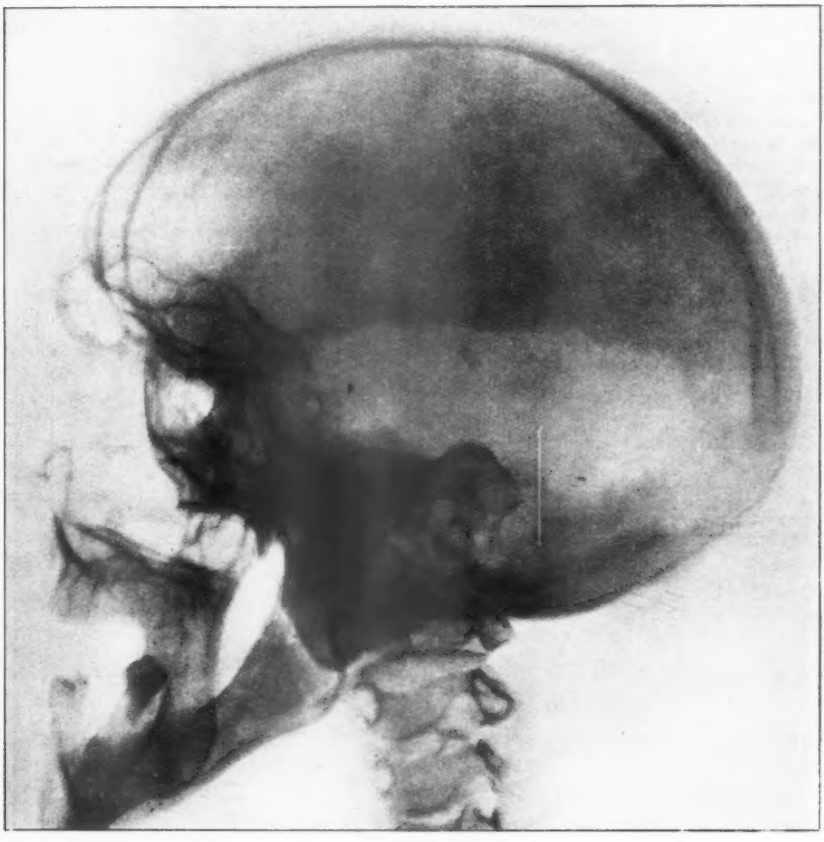


FIG. 2.

At the second operation the diseased bone yielded a mixed growth of *Streptococcus hæmolyticus* and large Gram-positive cocci.

On account of the thickening and whiteness of the dura, Wassermann and Kahn tests were done on two occasions, but they were negative.

The Value of Radiography in Symptomless Mastoiditis.

By T. B. LAYTON, D.S.O., M.D.

THERE are no symptoms of inflammation of the mastoid diploë. Those which we use to make a diagnosis in acute disease are not symptoms of the inflammation of the osseous tissue, but of the spread of this inflammation locally to surrounding structures or generally by the blood-stream. In many cases there is no such spread. These are cases of symptomless mastoiditis. They are probably more numerous than

otologists have formerly thought. They can be recognized by X-rays. Every case of otitis media which is not well in a fortnight should be considered as a possible case of symptomless mastoiditis, and a skiagram should be taken.

At this stage the change seen is a blurring of the outline of the lamellæ of osseous tissue which form the walls of the mastoid cells. If this is seen the mastoid should be opened, and the diseased bone removed if there is any ear discharge. In this way one is almost sure of securing a healed drum-head with normal hearing.

At a later date sclerosis supervenes, with deposition of earthy matter. This can be recognized under X-rays. When it has occurred the performance of the simple operation indicated above is less likely to be successful. Therefore the operation should be performed before sclerosis has begun. If we did this we should probably eliminate those tragic cases of intracranial complications of the chronic running-ear in middle age.

I believe that this sclerosis begins about two months after the onset of acute otitis. In every case of acute otitis media, accompanied by symptomless mastoiditis, there are therefore two months in which to effect a cure: after that time the best chance has gone for ever. For a generation otologists have been pegging away at the naso-pharynx as the key position whence an acute inflammation of the middle ear degenerates into a chronic condition. I suspect that the other end of the middle-ear tract is more often the important one. Therefore, in a case of unhealed otitis media of recent date, an operation upon the tonsils or naso-pharynx should not be performed until a skiagram of the mastoid has been taken. If this shows evidence of changes in the diploëtic tissue, the operation must be done *not* upon the throat but upon the mastoid.

Two of the cases illustrated by Dr. Mann's skiagrams are good examples of symptomless mastoiditis. In one (J. H., girl, aged 5) the sole symptom was ear discharge; there was not even a rise of temperature. In the other (D. R., girl, aged 5) there was a rise of temperature, but the child was already desperately ill with scarlet fever and diphtheria, which were enough to account for that rise.

I wish to give one word of warning in the form of a question. In an acute otitis media is there always, or frequently, some inflammation of the mastoid bone which subsequently clears up? If so, we must be careful not to call this condition an acute mastoid and to consider that it needs operation. I believe that radiography will clear up this matter, and give some indication of the pathology of the bone in acute otitis media.

Discussion.—Mr. E. WATSON-WILLIAMS said that in just those cases of doubt in which additional help beyond clinical signs would be valuable, it was not forthcoming from radiography. In the second case, which he had now shown, and in three or four others, there was a general blurring of the cells and opacity in the skiagram, so that had he assigned weight to the skiagraphic evidence, he would have advised operation. In actual fact he did not operate and a perfect recovery ensued.

He did not agree with Mr. Layton that radiography would help a decision in most cases; in ninety-nine out of a hundred the diagnosis should be made on the clinical findings, and if, three weeks after the onset the condition was not improving, active measures should be taken whatever the skiagraphic findings.

Mr. ALEXANDER R. TWEEDIE said he was sure that Mr. Layton did not mean that we should rely entirely on a skiagram for this purpose. Examination of the aural fundus, the condition of function, and of the patient generally, were the most valuable guides.

Mr. T. B. LAYTON (in reply) said that the kind of case in which he found radiography valuable was one in which there was no other evidence of inflammation of the mastoid bone. There would be a variety of opinion as to the value of that evidence. He was interested to learn that Mr. E. Watson-Williams did not find radiography of much value in doubtful acute cases, which were becoming semi-acute. It was when a symptomless case was threatening to become chronic that radiography was of value. Dr. Mann and himself had purposely brought up some cases in which the decision, judged by the skiagrams, had been wrong, i.e., in two of

the eight or nine shown. In one, operation was refused, and the patient recovered in spite of that refusal. In the other, the mastoid when opened, appeared normal and no organism could be cultivated from the piece of bone removed. In both of them the mastoid was of the infantile type, in which type it was more difficult to make accurate deductions from the appearances.

He did not think it was opening the antrum and affording post-aural drainage of the middle ear which was the valuable thing. The views he was developing with regard to the symptomatology of mastoid affections and the value of radiology were based on Dr. Dan McKenzie's recommendation, made some years ago, to open the mastoid if the middle ear did not heal. He did not think that when there was no disease of bone, post-aural drainage got rid of the disease. If there was disease of the bone, removal of that disease enabled the patient to get well. If there was not disease of bone, he doubted whether drainage did much good. In cases with ears which had been discharging for some time, more evidence was needed to tell which had some bone inflamed, and which had not. That evidence was supplied by radiography. Before an X-ray plant was installed at the Metropolitan Asylums Board[1] he had tried opening of the mastoid when the ear did not get well. In two he had chanced to find a small focus of disease and these cases were great successes. In the others, the mastoid was normal and none of them recovered. That was the type of case in which he advocated the taking of a skiagram before taking out tonsils. When one saw tonsils which one would remove whether there was a running-ear or not, he admitted that removal of those tonsils might give the running-ear a chance of getting better; but if there were tonsils which one would not remove except because of a running-ear, he had never known of a case in which removal had done good.

Some Notes on the Diagnosis of Acoustic Tumours.

By T. H. Just, F.R.C.S.

The rarity of this condition is the justification for this paper. All my conclusions are drawn from the clinical notes of the cases, made during the routine examination of the patients.

They are based on a series of 33 histologically proved cases, which I have seen at the National Hospital during the last six years. This comparatively large number gives one some fair grounds for dogmatizing on the relative frequency of occurrence of the various signs and symptoms. I shall also, for the purpose of differential diagnosis, refer to 3 cases of endothelioma of the dura mater of the lateral recess and also to 2 cases of cholesteatoma of the lateral recess, that rare tumour one sometimes sees growing from the dura mater.

In spite of the rarity of the condition, any otologist must, at some time or other, see cases of eighth-nerve tumour, sometimes at first hand, as some patients at the beginning complain of purely otological symptoms such as deafness, tinnitus, and giddiness, and as in some of these cases, the deafness is of a middle-ear type, it behoves the otologist to investigate the aural condition completely.

I do not propose to discuss all the neurological findings which occur. From the welter of sometimes contradictory findings, I shall confine myself to the more striking and constant symptoms which an otologist can recognize. The average otologist has neither the training nor the time, to make a detailed neurological examination of a doubtful case of trouble in or near the lateral recess, and from the wealth of signs elicited, always to draw a right conclusion.

The incidence of the condition is as follows: *Sex.*—Female, 24 cases; male, 9 cases. *Age.*—Three patients under 20 years (youngest 18); 12 between 30 and 40; 11 between 40 and 50; 5 over 50 (oldest 62).

The duration of symptoms before the patient was examined varies from one month to five years. This period is indefinite, as symptoms such as deafness of long standing, are probably due to some other cause.

1 Ref., M.A.B. Reports, 1922.

The following is a list of symptoms complained of by the patient himself, in the series of 33 cases, with their frequency of occurrence:—

Headache	25	Vomiting	15
Failing vision	22	Falling or lurching	23
Diplopia	12	Paresis—	
Giddiness	18	(1) hand or arm	10
Deafness	26	(2) leg	5
Tinnitus	16	Slurred speech	4
Sensory disturbances (practically all of upper fifth distribution)	14	Facial spasm	3

The most common symptom was deafness, and seven patients who did not complain of loss of hearing were found, on examination, to be suffering from unilateral deafness. Deafness may therefore be taken as constant. Headache in a large number of cases was occipital, but in others was general or even frontal. There was loss of tone in the arm or leg of more patients than are grouped under the heading of paresis. This loss of tone was illustrated in the case of the arm by a certain clumsiness in the performance of definite repeated movements, such as the finger-nose-finger test; and in the case of the leg, in the inability of the patient to stand steadily upon the affected foot.

CASES OF ENDOTHELIOMA AND CHOLESTEATOMA.

Symptoms	Endothelioma (3 cases)	Cholesteatoma (2 cases)
Headache	3	2
Tinnitus	3	1
Deafness	3	2
Giddiness	3	1
Failing vision	2	1
Lurching	2	2
Vomiting	2	2
Diplopia	1	0

N.B.—In one case of cholesteatoma, there was definite diminution of function of the homolateral vestibular nerve.

Thus it appears from the differential diagnosis point of view, that the symptoms complained of in cases of lateral recess tumours not connected with the eighth nerve are practically the same as those of definite eighth-nerve tumours.

Signs of Eighth-Nerve Tumour.—These may be divided into (1) those connected with the eye, (2) those connected with certain cranial nerves, especially the fifth, sixth and seventh, (3) signs of cerebellar involvement, and finally (4) the findings on examination of the eighth nerve.

Vision.—Sight varied from normal to complete blindness in 20 cases in which the vision has been recorded. Of these: In 1 case sight was normal; in 7 cases sight was equal in both eyes; in 6 cases sight was less on affected side; in 7 cases sight was less on contralateral side. It will be seen from this that except for the fact of loss of vision, the degree is of no help towards lateralizing the tumour.

Papillœdema.—Present in 27 cases; not present in 3 cases; no record in 3 cases. Papillœdema varies from 0·5 D to 5 D. Less on affected side in 13 cases, equal on both sides in 7 cases, greater on affected side in 7 cases. The intensity of the papillœdema does not appear very helpful in lateralizing the tumour.

Visual Fields.—Reduced in 8 cases, particularly to colour; on the affected side (4 cases), both sides (2 cases), contralateral side (2 cases).

Spontaneous Nystagmus.—Present in all 33 cases; coarse on deviation towards the side of tumour and fine towards the contralateral side (26 cases); fine towards the side of tumour and coarse towards the contralateral side (4 cases); fine to both sides (2 cases); fine nystagmus on deviation to the side of the tumour, with no nystagmus to the opposite side, in one case only. In 15 cases there was a fine, jerky nystagmus on looking upwards and downwards, sometimes slightly rotatory in

character. This proportion of a slow coarse nystagmus towards the side of the tumour is what one would expect, considering the relation of the tumour to the cerebellum.

Corneal Reflex.—Absent in 14 cases, diminished in 16 cases. No record in 3 cases. It is seen from this that diminution or absence of the corneal reflex is present in every case examined.

Sensation.—In 18 cases there was a diminution in sensation of cotton-wool and pin-prick over the area of the upper fifth nerve of the homolateral side. In some few cases the diminished sensation was more widely spread, and in one extended to the whole homolateral side of the body.

External Rectus Paresis.—On the side of the tumour (8 cases), on both sides (3 cases), on the contralateral side (1 case). Weakness of the rectus on the same side, therefore, appears to be of diagnostic help in lateralizing the condition.

The Facial Nerve.—Facial weakness occurred: On the side of the tumour (16 cases), on the contralateral side (2 cases). Facial spasm in 3 cases on the homolateral side. Facial weakness may therefore help in the diagnosis of the condition.

Palate showed weakness on the side of the tumour in 3 cases.

Tongue.—In one case the tongue was protruded to the side of the tumour.

Decrease of Power in Arm and Leg.—Arm: Decrease of power on the side of the tumour in 16 cases. To this must be added some which showed lack of accuracy in constantly repeated movements. Leg: In 9 cases there was weakness of the leg on the side of the tumour.

Position of Head.—Chin directed away from the side of the tumour (7 cases), towards the side of the tumour (3 cases).

Falling Reactions.—Patient veered or fell to the side of the tumour in 11 cases: to the contralateral side in 2 cases; both ways in 2 cases. Unsteadiness on homolateral foot in 20 cases.

Skiagram.—In 14 cases in which reports on skiagrams were included in the notes, 4 cases showed enlargement of the internal auditory meatus and 10 showed no change.

I have rather stressed the signs found on examination of the eyes, as in my opinion, they are of the greatest importance. I have omitted notes of the various reflexes found, as I think they are rather neurological than otological.

The Eighth Nerve.—Cochlear branch: (1) I have only detailed notes on the ears in 29 cases. Of these there was absolute deafness (13 cases), some loss of bone conduction (8), middle-ear deafness (8).

The fact that middle-ear deafness is present in so many cases is, from the point of view of diagnosis, disturbing. There may be some loss of function of the nerve, but if, on examination, it is found that air conduction is less than bone conduction, the Weber is referred to the deaf ear and a tuning fork placed on the affected mastoid is heard when a noise-box is sounding in the opposite ear, then one is forced to the opinion that one is dealing with a case of middle-ear deafness.

Method of Testing the Eighth Nerve.—The method which I personally find gives the most consistent results, and I have in all cases tried to make the method as simple as possible.

In testing the cochlear division I use only a heavy middle fork and a noise-box. Patients with a papilloedema of 2 to 5D are not good witnesses, and I do not think that very detailed testing of exact hearing or tone range can be looked upon as accurate in many of these cases. When the patients have absolute deafness it is easy, but to be certain of a small diminution of the bone conduction, when the Weber is referred to the good ear, or in mixed deafness, is, in many cases, not an exact scientific fact, but a matter of opinion. Still, I hold that by these simple methods—used with discretion—one can practically always determine the type of deafness, if not its exact degree.

Vestibular branch: All cases tested showed diminution or complete loss of the function of the eighth vestibular branch. The difficulty of testing the majority of these patients for the function of this branch lies in the fact that they all exhibit spontaneous nystagmus, practically always in both directions and varying in degree. Many of them are giddy, and some of them fall on standing with their feet together. Again, I do not dogmatize on which is the test of election. I shall merely relate the methods I use.

Rotation Test.—I find this test applicable to so few cases that I have ceased to use it, as I could never satisfy myself that the added nystagmus on swinging one way was of longer duration than the added nystagmus on swinging in the opposite direction, when there was a marked spontaneous nystagmus. Also, the differential falling and giddiness between the two sides was difficult to be sure of in patients who were spontaneously giddy and who had a weakness of the homolateral leg.

The Galvanic Test.—I have always found this galvanic test rather uncertain. At times it seems difficult to bring off, the nervous patient complaining of pain before nystagmus or swaying appears. Again, it has been shown that sometimes, at any rate, the galvanic test stimulates centres in the brain stem and not the nerve. The nystagmus caused by the galvanic stimulation is nothing like as marked as that obtained by prolonged stimulation with cold, and in view of the spontaneous nystagmus, which is always present, it is I think, almost impossible to determine whether there is any added nystagmus. The sway, when it occurs, is most typical and conclusive (though not necessarily of a functioning eighth nerve). The absence of a sway is not so conclusive. It may be due to my faulty technique, but I have never felt absolutely certain of the galvanic test. I have used it often in cases of eighth-nerve tumour, and have found it useful, in conjunction with the cold caloric test, in cases in which there was evidence of old suppurating or obsolete otitis media, in which one could not be sure otherwise that the labyrinth had not been destroyed by disease.

Cold Caloric Test.—I have found this the most useful test of the eighth nerve, as in my opinion it practically never fails. The nystagmus produced on prolonged stimulation is very marked and of wide excursion, the sensation of giddiness in normal patients is also well marked, typical labyrinthine falling reactions may readily be elicited, and errors in past-pointing are usually quite definite. One stimulates the affected ear and the affected ear alone, with the cold caloric test. Even with the cold caloric test in some difficult cases, there is so much spontaneous nystagmus, giddiness and falling, that the question as to whether the eighth nerve is functioning or not, is a matter almost of opinion, rather than of fact. I should like to emphasize this point, and it would be simplest if I quote the findings on testing the eighth nerve in some cases which were definitely proved to suffer from eighth-nerve tumour.

(1) Left membrane scarred. Weber to left. Vibrating fork heard over left mastoid, with noise-box in right ear. Apparently middle-ear deafness. Cold caloric test, left. Apparently no added nystagmus, no giddiness or falling reaction. ? "Dead left vestibular nerve."

(2) Some loss of inner-ear hearing (left.) Not by any means absolute. Cold caloric test (left); impossible to detect added nystagmus, as the spontaneous nystagmus is so marked. After prolonged syringing, no giddiness, nausea or falling. Left vestibular eighth is at any rate hyposensitive, if it is functioning at all.

(3) Left ear, cochlear division, eighth, not functioning. Cold caloric test, left, no added nystagmus, giddiness or falling. Past point touch. Galvanic test, left, no reaction or swaying; right, no very convincing sway. "I think the left eighth nerve is not functioning."

(4) Left ear, membrane very dull. Very deaf. Weber to right. Spontaneous past pointing, touch both hands. Does not fall. Cold caloric test, left. "I cannot

satisfy myself that there is any added nystagmus with the head in any position." Past pointing touch both hands, no falling, nausea or sensation of giddiness.

(5) Left ear, membrane thickened and retracted. Patient very deaf. Impression that there is nerve deafness. Spontaneous nystagmus with head in all positions. Falling backwards and to the left with all positions of the head. Past pointing, eight inches outwards with the left hand. Cold caloric test, left. "I cannot satisfy myself that there is any added nystagmus for any position of the head." There is practically no giddiness. The past pointing and falling are the same as before stimulation. "My impression is that the left eighth vestibular nerve is not functioning."

(6) Right ear, slight deafness. No loss of high or low tones. Cold caloric test very sluggish and practically no giddiness or falling. With galvanic test, sways alternatively to right and left, on receiving current added nystagmus in both directions during stimulation with either pole. (Tumour the size of a cherry growing from eighth nerve.)

It will be seen from these reports, that the cold caloric test may be of help when the galvanic test is uncertain. Again, these cases show the difficulty in judging whether there is added nystagmus or not on stimulation, and show the importance of the loss of sensation of giddiness, falling and past pointing, as aids to determining whether the eighth-nerve vestibular branch is functioning or not.

Let us now try to gain some sort of clinical picture of a case which may be that of an eighth-nerve tumour. The patient exhibits the following signs and symptoms: Deafness, spontaneous nystagmus, loss or diminution of the corneal reflex, papillœdema, loss of vestibular function. If to these findings there are added any or all of the symptoms and signs, already described, then the case is almost certainly one of tumour of the lateral recess, and with involvement of the eighth vestibular branch it is almost certainly a tumour of the eighth nerve. Although some interference with the function of the eighth nerve may occur, in cases of extra-cerebellar tumours of the dura mater of the posterior fossa, merely from pressure, in all cases of acoustic nerve tumour the function of the vestibular branch is interfered with, even though the cochlear branch may escape, and therefore the findings in these cases, of a partly or completely damaged eighth vestibular branch, is for practical purposes pathognomonic of an acoustic nerve tumour.

In conclusion, I should like to thank my colleagues at the National Hospital for their kindness in allowing me to use the case notes of patients under their charge.

Tumours of the Eighth Nerve.

By J. S. Fraser, M.B., F.R.C.S.E., and W. T. Gardiner, M.B., F.R.C.S.E.

During the years 1918 to 1928 (inclusive) 13 suspected cases of eighth-nerve tumour were seen in the Ear and Throat Department, Royal Infirmary, Edinburgh. In 8 of these the diagnosis was definitely confirmed by operation or post-mortem findings.

Sex.—Of our 13 cases, 11 were females and only 2 were males. *Age.*—3 of our patients were under the age of 21 years; 6 between 31 and 41, 2 between 41 and 51, and 2 just over 51.

Infection.—None of our cases had evidence of middle-ear suppuration. In 9 cases the drumhead on the affected side was normal, and in the remaining 4 only slight opacity and indrawing were noted.

Side.—It is interesting to note that in 9 of the cases the right side was affected, in 3 the left, while in 1 case the tumour was bilateral. (Case improving.)

Symptoms.—As the subject is being treated from the otologist's point of view, symptoms which arise in connection with the eighth nerve will naturally fill the picture and are dealt with first.

Eighth Nerve (*Cochlear Division*).—It must be admitted that it is difficult, or impossible, in many cases to obtain an accurate chronological history of the onset of the symptoms. Patients with unilateral deafness may for long periods fail to notice it when the hearing in the other ear is normal. It is usually stated, however, that deafness is the first symptom, generally accompanied by noises. In all our 13 cases the patients complained of deafness, but in only 2 was tinnitus noted. In the 8 cases in which the watch was employed in the examination, it was noted that it was not heard, either by air or bone-conduction, on the affected side. In the 6 cases in which the Rinne test was employed, it was found that while the tuning fork was not heard at all by air conduction, it was heard by bone-conduction almost certainly in the sound ear, i.e., Rinne's test was "absolute negative." In the 5 cases in which Weber's test was employed, the fork was lateralized to the good ear. When the higher-pitched forks, 1024, 2048 and 4096, were held opposite the affected ear, the patient said that she could hear them, but if the noise box was going in the good ear the patient could not hear them. Voice test: With the noise box going in the good ear twelve of the thirteen patients were absolutely deaf; the remaining patient heard the distinct voice at a foot.

Vestibular Division.—Giddiness was noted in 9 of the 13 cases: in one case giddiness came on before deafness.

Vestibular Tests.—Spontaneous nystagmus to both sides was present in 5 cases: spontaneous nystagmus to both sides, along with nystagmus on looking upwards, was noted in 7 cases, while in the remaining case there was spontaneous nystagmus to both sides and nystagmus on looking down. This symptom, spontaneous nystagmus to both sides, with vertical nystagmus—appears to us to be the most valuable of all in the diagnosis of eighth-nerve tumour, at least so far as otological examination is concerned. In 2 of our cases the nystagmus was most marked to the opposite side and in another 2 to the same side. This accords with the findings of other observers, though Cushing believes that the nystagmus is more marked when the patient looks towards the side of the lesion.

Spontaneous Pointing Error.—The absence of this is also a pronounced feature. Spontaneous pointing was normal in at least 11 of our 13 cases. This is in marked contrast to the conditions found in cerebellar abscess and intra-cerebellar growths.

Rombergism is not a very noticeable feature. There was slight swaying on this test in only 5 of the 10 cases in which the condition was noted, and it was definitely absent in 2.

Rotation Test.—We have not employed this test, as it is very difficult to observe the result in cases of eight-nerve tumour on account of the spontaneous nystagmus.

Galvanic Test.—It has also been found difficult to obtain satisfactory results by this test, not only in cases of eighth-nerve tumour, but in other conditions. Patients almost always complain of such severe pain that the current has to be reduced and stopped before nystagmus is produced; indeed, the only condition in which a satisfactory nystagmus has been produced on the galvanic test is that of chronic middle-ear suppuration with large perforation of the drumhead, in which zinc ionization treatment is used.

Cold Caloric Test.—This is important. In view of the presence of spontaneous nystagmus to each side, it should of course be carried out with the eyes looking straight forward. The reaction was found to be absent in 10 of the 13 cases. In the other 3 the test could not be carried out, as the patient would not allow it. In 2 of the cases it was noted that on syringing the sound ear a very marked and prolonged nystagmus was obtained; this agrees with Neumann's finding.

Nausea and vomiting were noted in only 5 of the 13 cases. It was definitely stated that there was no vomiting in 2, while in the remaining 6 there is no note under this heading.

Staggering and falling were present in 8 of the 13 cases, while in the remaining 5 there is no note. In one case the patient stated that she fell towards the side to which she attempted to turn.

Other Cranial Nerves. (I) In no case is there any mention of loss of olfaction. (II, III, IV and VI) 5 of the patients had optic neuritis. In 3 cases the patients complained of diplopia. (V) 9 patients complained of headache; in 2 of these it was definitely stated to be frontal. Only in 4 cases was there loss of the conjunctival reflex or diminution of the sense of touch on the cheek of the affected side. (VII) Facial paralysis was present in 7 cases, absent in 3, and in the remaining 3 there was no note, but it is almost certain that there was no facial weakness. Loss of taste on the affected side of the tongue was noted in 3 cases. (IX and X) In only 1 case was there difficulty in swallowing. Slow or slurring speech or difficulty in articulation were noted in 5 cases. In 2 cases there was paresis of the palate. In the 4 cases in which the larynx was examined there was no abnormality. (XI) In no case was there any abnormality of the sterno-mastoid or trapezius muscles. (XII) In no case was there any hemiatrophy or difficulty in protruding the tongue.

The *pronation and supination test* was only noted in 2 cases, in which there was fairly well-marked dysdiadokokinesia on the homolateral side.

Increased *tendon reflexes* on the contralateral side were noted in 3 cases, while tremor of the upper extremities was noted in 2 cases.

In all cases tested, the Wassermann reaction was negative.

In several of the cases X-ray examination of the temporal bone was carried out in the oblique lateral position to show the internal meatus superimposed on the external meatus. In none did the radiogram give any definite evidence of enlargement of the internal acoustic meatus. In two cases which we are allowed to quote by kind permission of Mr. Dott, X-ray examination was of the greatest use.

Differential Diagnosis.—Eighth-nerve tumours have to be distinguished from: (1) Acquired syphilitic affection of the labyrinth and eighth nerve, including syphilitic basal meningitis (Wassermann test).

(2) Neuritis of both divisions of the eighth nerve which rarely causes complete permanent deafness and loss of vestibular reaction.

(3) Serous meningitis in the lateral cistern, and various forms of labyrinthitis associated with suppurative otitis media, and therefore unlikely to be mistaken for eighth-nerve tumour.

(4) Ménière's disease: here again complete deafness and absence of vestibular response are almost unknown. The presence of choked disc would negative Ménière's disease.

(5) Multiple sclerosis, bulbar paralysis and locomotor ataxia: the diagnosis of these diseases falls to the neurologist rather than the otologist.

(6) Tumours of the cerebellum: in these one would expect to find a well-marked pointing error, which is absent in eighth-nerve tumours.

(7) Cerebellar cyst.

The following case is quoted in full to show the difficulty in making a diagnosis of eighth-nerve tumour before the appearance of (?) neurological symptoms:—

T. B., male, aged 57, seen May 8, 1925, complaining of attacks of giddiness and vomiting during the previous five years. Also complained of deafness and continuous noises in left ear of three years' duration. Wassermann reaction negative.

On examination: Drumheads were normal. Watch heard on right mastoid but not on left. Rinne's test absolutely negative on the left side and no tuning forks could be heard by the left ear with the noise box in the right. Further, the patient was quite deaf with the

noise box in the right ear. There was some spontaneous nystagmus both to right and to left, most marked to right. There was no pointing error and very little, if any, Rombergism. Cold syringing of the right ear produced the normal reaction, whereas cold syringing of the left ear produced no nystagmus even in three minutes.

Examination of the nervous system was negative. There was no indication of involvement of any other cranial nerves. The fundus oculi was normal. Radiograms did not show any dilatation of the internal meatus on the left side, The electrical reaction on the right side was normal but no reaction was obtained from the left ear.

The radical mastoid operation was performed by J. S. F., followed by Neumann's labyrinth operation, with division of the seventh nerve on the affected side and opening of the internal acoustic meatus. No tumour was found. Meningitis supervened eleven days after operation, and the patient died on the fifteenth day. Post-mortem showed meningitis only.

To summarize:—

Acusticus tumour should be suspected in a case in which there is absolute loss of cochlear and vestibular function, accompanied by (?) spontaneous nystagmus in all directions, i.e., lateral and vertical, but with no spontaneous pointing error or Rombergism. It follows also from what has been said regarding cerebellar cysts that a definite diagnosis cannot be made before the appearance of neurological—as apart from otological—symptoms unless X-ray examination shows dilatation of the internal auditory meatus on the suspected side.

Discussion.—Sir JAMES DUNDAS-GRANT said that he would urge more strongly than Mr. Just did, the value of the galvanic test. It should, however, be unilateral only, with the cathode pole on the back of the neck and the anode pole on the ear. Then with very few amperes there should be produced a definite sway towards the anode. It was in the cases in which the disturbance was not very advanced that one wanted to make a diagnosis, and it was there the method was of use. For the caloric test he recommended his cold-air apparatus. Mr. Sydney Scott had said that this gave positive results when cold water did not, and was not so likely to be refused by the patient. In all cases of obscure nerve deafness the corneal reflex should be tested; this would put one on the track of a pontine-cerebellar tumour at an earlier stage than would otherwise be the case. The galvanic current need not be used to the extent of producing nystagmus, as that required 10 to 15 milliamperes and caused pain. In the absence of labyrinthine reaction one wanted to know how the nerve reacted, and the galvanic test told us this.

Mr. ALEXANDER R. TWEEDIE said he noted with regret that these authors also had not found the rotation tests of much value, but he himself still carried out these tests, hoping that they might yet prove of diagnostic value.

He, too, had been rather disappointed in the caloric and galvanic tests, until he realized that the value of responses had a direct relation to the fineness of the resistance of the electrical apparatus in the galvanic tests, and to the minimal amount of cold water used in the caloric test.

With the galvanic test, in physiological cases, the leaning effect was produced before the nystagmus, whilst in pathological cases this sequence was sometimes reversed.

The cold caloric test was chiefly of use in indicating the functional integrity of the peripheral organ, whilst the galvanic test was solely a test for the vestibular nerve *and* probably its distal ganglia, as pointed out in a recent paper by Dr. Gösta Dohlman. ("Experimentelle Untersuchungen über die galvanische Vestibularisreaktion," *Acta Oto-Laryngologica*, 1929, Suppl. viii, 48). He agreed with Mr. Gardiner that these tests should never be restricted to the side in question; their value was largely dependent on the result of a general systematic bilateral examination.

Mr. SYDNEY SCOTT said that many cases of deafness might be associated with a peripheral lesion of the vestibular nerve, as Mr. Tweedie had said, so that there was a negative caloric reaction, but a positive galvanic reaction. He (the speaker) had also seen many cases of lateral recess tumours which, upon operation, had proved to be cases of auditory nerve tumour. In all of them there was a negative galvanic reaction on the side of the lesion. In one case there was no galvanic reaction on either side, and that patient had bilateral auditory nerve tumours.

[Mr. TWEEDIE: If the resistance is adjusted the galvanic test will not cause pain.]

Mr. BROUGHTON BARNES said Mr. Just's statement that eight out of thirty-three cases had middle-ear deafness caused him (the speaker) some anxiety with regard to diagnosis.

Had Mr. Just found any marked changes in the middle-ear in those cases? or could he give any explanation of the fact?

Mr. E. WATSON-WILLIAMS [communicated later]: The explanation of the *conduction* deafness observed in some of Mr. Just's cases in which there was little or no *perception* deafness, may possibly be found in the "choked labyrinth," of which examples were shown at the meeting; that is to say, in an exudation of lymph into the scala tympani and scala vestibuli, the organ of Corti escaping damage. The condition would then be that described by Claoué[1] as "humoral deafness," a deafness due to alterations in the perilymph, and characterized by tests indicative of conduction deafness.

Mr. JUST, in reply, repeated that he did not wish to decry the galvanic test, but simply to say that in his own experience he found it less reliable than the cold caloric test. In many cases he used both. In cases in which there was a marked spontaneous unsteadiness on standing, and one could not be sure of the presence of added nystagmus, by the more violent stimulation of the cold caloric test one could judge whether the patient became giddy and had pointing reactions, better than one could with the galvanic. He always used one electrode strapped on the head, the other on the wrist of the same side, so that the patient was clear of the stimulator. He usually tested both sides, in order to compare the responses of the normal and the affected areas.

Until he looked up his cases he had not realized that deafness in the affected ear occurred so often. He could not be certain, in most of those cases, whether there was a slight degree of nerve deafness. In the cases of eighth-nerve tumour the drum might be dull and slightly retracted, but usually no definite change was present.

Mr. W. T. GARDINER, in reply, said that both Dr. Fraser and himself found the cold caloric test of much more value than the galvanic.

Fibroma of the Eighth Nerve simulating a Tumour of the Cerebellum. T. B. JOBSON, M.D.—E.C., married woman, aged 31, admitted to Guildford Hospital, January 21, 1929, on account of failing vision.

History.—Initial symptom was deafness, beginning on right side two years previously, increasing mental dullness (three months), vertigo, falling forward and to right, attacks of headache and vomiting (six weeks).

Physical Signs.—Vision: right $\frac{6}{36}$, improved with glasses to $\frac{6}{24}$; left $\frac{6}{12}$, improved with glasses to $\frac{6}{9}$. Papilloedema, right and left about 2 D. Pupils dilated; right does not react to light. Double ptosis, paralysis of right sixth nerve. Coarse symmetrical horizontal nystagmus. (Dr. R. Lang.)

Central Nervous System.—Right corneal reflex absent, deviation of jaw to right side. Knee-jerks, right +, left ++. No ankle clonus. Plantar reflexes absent. Abdominal reflexes (?). No Kernig's sign or head retraction. Generalized incoordination and muscular atony. Mental condition, "very lethargic, almost stuporose." (Dr. A. F. Tredgold).

Ears.—Membranes show evidence of catarrhal changes; both dull, right retracted. No evidence of suppuration. Patient's mental condition precluded any accurate hearing tests. Could hear loud voice with left ear, but nothing with right.

Abdomen, heart and lungs normal. Wassermann reaction negative. Slow pulse (60).

Diagnosis.—Tumour of right auditory nerve, confirmed by stereo-radiogram.

Operation (Mr. G. H. Steele, F.R.C.S.).—Bilateral posterior fossa decompression, using Cushing's cross-bow incision. Occipital bone between and below lateral sinuses removed, including posterior margin of foramen magnum and posterior arch of atlas, to relieve pressure of the large medullary cone which was present. Palpation revealed a nodular circumscribed tumour $\frac{1}{4}$ in. below the surface of the cerebellum apparently completely imbedded in the right lateral lobe. Retraction of the cerebellum was begun with a view to inspecting the eighth nerve, but before the internal auditory meatus was reached, free hæmorrhage put a stop to the operation

1 Claoué, "Les Surdités Humorales," *L'Oto-rhino-laryngologie internationale*, July, 1924, 373.

and the wound was closed. After an interval of six weeks the wound was reopened. A typical auditory fibroma, the size of a hen's egg was found, occupying the cerebello-pontine angle, having been extruded from the cerebellar substance. The tumour was now completely free from the lateral lobe of the cerebellum. Intracapsular removal by morcellement was commenced, but free hæmorrhage again obscured the field and extracapsular enucleation with the finger was now resorted to, the tumour coming away quite readily. Hæmorrhage, however, was controlled with difficulty and the patient died a few hours after the operation.

Remarks.—From the point of view of radical operation, the differential diagnosis of tumours in the posterior cranial fossa resolves itself into the distinction between the two commonest groups of neoplasms which are found there, namely tumours of the cerebellum and fibromata of the eighth nerve. The importance of this differentiation is that apart from simple cysts the majority of growths in the first group are not amenable to extirpation, whereas most auditory fibromata can be removed to a greater or lesser extent. In some cases the distinction is easy, but extracerebellar tumours may give rise to symptoms of pressure on the cerebellum, while true cerebellar tumours may involve the other structures, such as cranial nerves, in the posterior fossa. This being so, the diagnosis is not always supported by the operative findings and this case illustrates this point.

The interest of this case lies in the apparent confutation of the diagnosis by the fact that an extracerebellar neoplasm had buried itself in the cerebellar lobe, by a process similar to that by which an endothelioma of the dura mater embeds itself in the cerebral substance without infiltrating it. The tumour, felt through a thin surrounding layer of cerebellum, had simulated exactly a tumour in the very centre of the lateral lobe. It was also extremely interesting to observe the effects of the extrusive powers of the cerebellum, when brought into play by the release of pressure consequent upon decompression. The brain substance had expelled the foreign tumour, and in doing so had attempted to approximate to the normal condition of affairs in the posterior fossa [G. H. S.].

Pathologist's Report on the Tumour.—Size, 3 in. by 2 in. by 1½ in., encapsulated, lobulated. Homogeneous throughout on cross-section, with several hæmorrhages of varying sizes. Section, stained hæmatoxylin-eosin, shows the characteristic reticulum with glial or pseudo-glial fibrils. Nerve-fibrils are very scarce. The fibrous bands throughout show a whorled appearance, with fibroblasts in varying stages of maturity. Very little hyaline changes in the fibrous tissue, these being confined to the vessel-walls, being especially well seen in one of the larger vessels at the junction of the reticular and fibrous bands. Some areas of œdema in the reticular tissue, but this is not very marked.

The tumour appears to be a typical neuro-fibroma of the eighth nerve. [R. C. Matson.]

When a case of this kind comes to the ophthalmic department it is too late, because it means that pressure-signs have developed. It is to the otologist one has to look for the early diagnosis of the condition. The operation was one of great magnitude, and needed exceptional skill. Only by getting these cases early can the death-rate be reduced. In Cushing's clinic the death-rate has been reduced from 80% to 20% after many years of special experience, and this reduction is due to early recognition and careful elaboration of the technique. Cushing takes four hours to perform this operation.

Tumour of the Nervus Acusticus demonstrated by Radiography.—D. A. IMRIE, M.D.—X-rays have been used as an aid to diagnosis of eighth nerve tumours, to show destruction of bone about the internal auditory meatus of the affected side.

The majority of eighth nerve tumours appear to arise in or about the internal auditory meatus, and cause irregular enlargement of the canal or destruction of the surrounding bone.

The difficulties which the radiologist has encountered are: (1) The deep situation of the petrous portion of the temporal bone does not permit a very clear delineation of the bone structure on the film. (2) It is almost impossible to produce symmetrical views of the two sides when attempts are made to pass the beam of X-rays along the internal canals. Mistakes have arisen when the external canal has been regarded as a dilated internal canal.

Both Cushing and Henchen have remarked on the unsatisfactory information afforded by X-ray examination in these cases.

Conte, of Turin, suggested the transorbital view, in which the beam of X-rays passes through both orbits, and the petrous bone of both sides is shown on one film.

The case demonstrated was diagnosed from films produced by this projection, using stereoscopy. As there was a considerable destruction of bone, the diagnosis was made with assurance. At the preliminary operation of decompression, the tumour could be felt in the cerebellum, under the dura, and doubt was thrown on the accuracy of the diagnosis. The subsequent operation verified the diagnosis.

The value of this projection of Conte is that truly symmetrical—and therefore comparable—views of the petrous bone on both sides can be obtained on one film. Supplemented, as he recommends, by a view with the mento-vertex-plate projection, in favourable cases, good views of all three semicircular canals and two views of the cochleæ are shown.

Objective Tinnitus.—G. GILL-CAREY, F.R.C.S.—Mrs. S., seen in May, 1929, complaining of severe tinnitus. A crackling sound, not synchronizing exactly with the pulse, could be heard by the unaided ear a foot away from the patient.

There was no clonic contraction of the palatal muscles, and the left Eustachian tube, seen through the naso-pharyngoscope, was normal. Pressure on the carotid artery did not modify the sound.

Radiographic examination of the left temporal bone by Dr. H. Graham Hodgson showed no abnormality. Wassermann reaction, negative.

Discussion.—Mr. O. POPPER referred to a case entitled "Nystagmus of the Tympanic Membrane" shown two years previously and said that he himself could voluntarily reproduce the condition, which was, he believed, due to the contraction of the tensor tympani.

Sir JAMES DUNDAS-GRANT said that in this case he had seen no movements of the short process of the malleus under the influence of the tensor tympani. He thought that no explanation of the condition was known.

Mr. L. GRAHAM BROWN said that he had shown a case, in a middle-aged woman, of both objective and subjective tinnitus which was like the cawing of a rook and could be heard with the stethoscope. There had been symptoms of increased blood-pressure, and the tinnitus had disappeared on pressure of the carotid artery on the same side and had therefore been labelled "arterial bruit."

Mr. A. D. SHARP said that years ago he showed a case in which the tinnitus could be heard about a foot from the patient. It had resembled the humming of a bee and the unfortunate patient had in consequence become known as "the man with a bee in his bonnet." He (Mr. Sharp) had observed that the frequency of the clicking noise in this present case was greatly reduced when the patient stopped breathing.

Sir JAMES DUNDAS-GRANT demonstrated on the screen the skiagrams from the case of a man who had fallen down and had remained unconscious for some time afterwards. There was complete labyrinthine deafness in the right ear. The question arose as to whether there had been an effusion into the labyrinth, due to the fall, or whether the fall had been due to the labyrinthine trouble. A line seen in the right orbit was considered by the radiologist to indicate a fracture.

Section of Tropical Diseases and Section of Pathology.

[*January* 7, 1930]

DISCUSSION ON TROPICAL DISEASES ARISING FROM DIETETIC DEFICIENCY.

Major-General J. W. B. Megaw: At the outset it is desirable to take a broad general view of the part played by dietetic deficiency in causing disease in the tropics. The three chief types of deficiency are: (1) Shortage of food as a whole. (2) Shortage of proteins. (3) Shortage of vitamins. As it was probably intended that this discussion should deal specially with the question of vitamin deficiency, I shall only make a passing reference to the other forms of dietetic defect, although I regard them as being of far greater importance.

Millions of people in the tropics live close to the border line of starvation even in normal years, so that when a harvest fails, there is actual destitution in those countries which have no provision for famine relief. The real problem for most people in the tropics is the adjustment of the population to the food supply. Sanitarians and research workers should recognize that their efforts to improve the conditions of human existence will be of little avail so long as every advance in disease-prevention is nullified by a corresponding increase in the population.

The well-being of a community rests on four supports—production, controlled reproduction, disease prevention, and the maintenance of personal security. If any one of these is allowed to become weak, the condition of the people is bound to be precarious. My reason for emphasizing these obvious points is that there has been a tendency for medical workers to rely on their own unaided efforts and to fail in their duty of educating Governments and peoples in the need for coördination of forces in dealing with the problems of human existence.

Next in importance to the provision of an adequate supply of food as a whole comes the necessity for a sufficiency of suitable proteins.

The work of McCay on the nitrogen factor in nutrition has demonstrated quite clearly that most people in the tropics suffer from a shortage of available proteins. McCay could find little evidence of vitamin deficiency in the diets which he investigated, and while I am far from desiring to minimize the importance of vitamin deficiency as a cause of disease, I believe that if we could assure an adequate supply of suitable proteins, the vitamins would take care of themselves to such an extent that they would no longer form a grave problem. It is possible to devise an experimental diet in which there are enough proteins and calories, and yet the vitamins will be quite inadequate for the needs of the body, but if we consider only the everyday diets of the people in the tropics, it is uncommon to find any that are well supplied with proteins and are deficient in vitamins alone.

Turning next to the question of vitamin deficiency, I will confine my remarks to the subject of vitamin B, as this is more than enough for one evening's discussion.

My chief object is to suggest that further investigation is likely to show, on the one hand, that this vitamin plays unsuspected parts in the causation of disease, and, on the other, that a deficiency is not responsible for the ill-effects that have been attributed to it.

We have many examples of the sway which is exercised by "fashions" in medical matters, and most people will admit that vitamins have become a fashion even in research circles. The vitamin-deficiency view of the causation of beri-beri has been exalted to the rank of a medical dogma, and anyone who dissents from it

is likely to come under the suspicion of the great sin of heterodoxy. The writers of textbooks are almost unanimous in their adhesion to the view that vitamin B deficiency is the cause of beri-beri, whereas most of the workers who have seen outbreaks of the disease refuse to regard deficiency as a complete explanation of the cases which they have met with, many even denying that it has played an important part in the causation of the outbreaks of which they have had personal experience. It is hard to account for this remarkable state of affairs on any grounds other than the attractiveness of clearly expressed dogmas.

We are all familiar with the reasons for the vitamin-deficiency view of beri-beri : the disease in the Far East has long been recognized as being closely associated with a diet of overmilled rice, and one of its most striking manifestations is polyneuritis. When it was found that avian polyneuritis could be caused by a diet of overmilled rice and could be prevented or cured by adding vitamin B to this diet it was natural to suspect that human beri-beri and avian polyneuritis were the same, and that both were caused by deficiency of vitamin B in the diet. Human experience seemed to supply final proof, for it was noticed that when groups of labourers suffered from beri-beri while living on a diet of overmilled rice, the disease could be controlled by supplying parboiled rice which is known to be rich in vitamin B. The weak point in connection with this human observation has been ignored. It is that if the cause of the disease was some positive factor like a poison in the kind of rice used, a change of rice supply would abolish the disease just as certainly as it would if the disease were due to deficiency of some essential food factor.

Let us turn for a moment to the attempts which have been made to reproduce the disease in human beings under experimental conditions. Strong and Crowell carried out an important series of experiments on condemned criminals in the Bilibid Jail in the Philippines. The prisoners were kept under strict control on special diets for more than seventy days ; all were kept on the same basic diet, which was poor in vitamin B ; in addition to the basic diet, some of the prisoners received overmilled rice, another group received overmilled rice and extract of rice polishings, while red rice was given the third group. It was expected that the prisoners of the first group would suffer from beri-beri while those of the other two groups would escape, but the actual results were that ten out of seventeen prisoners in the first group suffered from symptoms suggestive of beri-beri, while two out of six in each of the other two groups also suffered from similar symptoms, though rather less severely.

If we regard the disease as having been true beri-beri, the results are far from convincing from the point of view of the deficiency hypothesis, for seven out of seventeen persons whose diets were specially designed to cause the disease, escaped while four out of twelve suffered from the disease, although their diets contained adequate supplies of the vitamin. What the experiments really showed was that a monotonous diet, deficient in calories, available proteins and vitamin B, caused nutritional disturbances suggestive of beri-beri, and that a supply of vitamin B gave inadequate protection against these disturbances ; they also showed the difficulty of devising a diet defective in vitamin B, yet satisfactory in other respects. Strong and Crowell later said that vitamin B ought not to dominate the picture when it is a question of treating beri-beri. Other workers have failed to cause beri-beri in human beings by feeding them on diets lacking in vitamin B, and the only experiment for which success has been claimed in this direction is that of Taguchi who kept five persons on a diet of overmilled rice, with the result that in all the subjects cardiac dilatation developed within five days and anæsthesia of the arms within ten days. The rapidity with which the symptoms appeared is not in keeping with what we know of deficiency diseases, indeed there is a distinct suggestion of intoxication.

Then we have evidence which cannot be ignored, that many outbreaks of beri-beri have occurred among groups of people whose diets were beyond reproach in the

matter of vitamin B content, so that both human experiment and human experience are far from demonstrating the existence of a close relationship between beri-beri and deficiency in vitamin B. To suggest that all such outbreaks were of some disease other than beri-beri is to beg the question, for there is no evidence that they were not as much entitled to the name as any others.

My own experience of the subject deals chiefly with a number of outbreaks of epidemic dropsy, a disease which seems to have as much claim to be called beri-beri as the forms of the disease which are seen in the Far East; I have asked both Vedder and McCarrison whether they could suggest any reason for regarding epidemic dropsy as distinct from beri-beri, but neither of them could do so. Some of the reasons for asserting that epidemic dropsy is not a deficiency disease are: (1) The disease usually appears as an explosive outbreak among groups of persons who are living on the usual kind of diet, which differs in no obvious respect from that of their neighbours who remain quite free from the disease. (2) In several outbreaks it has been found that all the victims obtained their supply of rice from the same shop or store, while their neighbours who bought their rice from other sources remained quite healthy. (3) Most of the victims have been eaters of parboiled rice which is regarded as being rich in vitamin B. (4) In most of the outbreaks there has been no suggestion of any deficiency in vitamin B.

Here again the suggestion has been made that epidemic dropsy is quite different from beri-beri and that arguments based on observations of the disease do not apply to beri-beri, but even if we were to accept this view, we are still faced with the fact that there is a disease of rice-eaters which closely resembles beri-beri and kills or disables its victims just as effectively as that disease does. From the point of view of the working practitioner and of the patients it matters little whether we decide that the one name or the other should be applied to the disease, the results in either case remain the same.

There is much to be said for defining epidemic dropsy as the "beri-beri of eaters of parboiled rice."

A word must be said about the supposed identity of avian polyneuritis and human beri-beri. The manifestations of these diseases are strikingly different in several important respects. In the human disease there is dropsy and cardiac enlargement, while in the avian disease there is a drying up of the tissues and cardiac atrophy. It is true that McCarrison recently found cardiac enlargement in some pigeons which had been fed on a diet to which a small amount of vitamin B was added, and it is to be hoped that further experiments on the same lines will be carried out, as they may throw much light on the subject of avitaminosis and even of beri-beri, but of course, in the long run, what we must aim at is to find out how human beri-beri is caused and how it can be prevented.

Conclusions.

"Beri-beri" is a name which has been applied for many years to certain disease manifestations which occur for the most part among persons who eat rice; the rice which is associated with the causation of the disease has usually been stored in hot and damp places for considerable periods after manufacture. It is quite likely that two or more specific diseases are included in the beri-beri group, but these have not yet been differentiated from each other in a satisfactory manner. One of the diseases is probably caused by poison formed in manufactured rice by the action of micro-organisms which have not yet been clearly identified. As in the case with other forms of food poisoning, it is possible that toxic infection may play a part, but the evidence points to intoxication as being the more important factor. It is probable that some of the cases of a disease to which the name beri-beri has been applied are caused by dietetic deficiency and it is likely that vitamin B is the factor which is specially concerned.

As a working hypothesis we may assume that there are two diseases of the beri-beri group—intoxication beri-beri and deficiency beri-beri. The efforts of investigators ought to be directed towards differentiating these and other possible forms of beri-beri from each other and discovering the essential cause of each. Hypotheses which invoke several causes to account for one disease are unsatisfactory and suggest ignorance of the real cause, for although there may be a number of predisposing or auxiliary factors, it is highly probable that each disease has one essential cause. Some workers have even suggested that three distinct causes are at work in producing beri-beri, namely, vitamin deficiency, bacterial infection and endocrine deficiency. In this connection it is legitimate to ask why the endocrine glands have become disordered and to suggest that they may be "more sinned against than sinning."

Finally, medical practitioners need not be depressed by the difficulties surrounding the beri-beri problem, for if they adopt the lines of action indicated by our knowledge of the conditions under which the disease occurs, they will be able to handle effectively the cases and outbreaks which they encounter. In treating the disease they will cut rice out of the diet and so ensure the elimination of any poisonous substances which may be present; they will also prescribe a diet rich in vitamin B and in all the other health-forming constituents. In preventing the disease they will aim at securing satisfactory conditions for the manufacture and storage of the rice so as to retain the nutritive properties of the grain and prevent the formation of toxic substances; at the same time they will attend to the diets of the people for whom they are responsible and will see that these are well provided with all essentials. Each of these methods of dealing with the disease is inherently reasonable, whatever our views of the causation of beri-beri may be, and it is quite certain that their adoption will lead to its control.

All medical practitioners who have opportunities of observing diseases of the beri-beri group should make careful inquiries into the conditions under which the disease occurs and should keep careful records of its clinical manifestations. Far too often we are told that "so many cases of beri-beri occurred" and receive no information regarding clinical features, so that it is impossible to form an opinion as to the type of the disease. If we insist on regarding beri-beri as a name given to a group of diseases whose members have not been clearly differentiated from each other it is likely that real progress will be made in our knowledge. What has been said of beri-beri applies to a great extent to pellagra.

Dr. G. M. Findlay: Our knowledge of deficiency diseases is derived from two sources: (1) the study of certain diseases occurring in the human subject, and (2) nutritional experiments on animals, conducted in the laboratory.

Before discussing the pathology of those nutritional deficiency diseases which can be produced in the laboratory and which throw considerable light on the ætiology of deficiency diseases in man, it will be well to mention briefly the present state of our knowledge in regard to the constitution of an adequate diet. Broadly speaking, there are two main forms of inanition. The first is the quantitative type, in which all the known necessary food constituents are present in the food, but the amount of the food is insufficient both for the growth and repair of the tissues and for the maintenance of energy. The second form of inanition comprises the various qualitative deficiencies in which there may be complete or incomplete absence of one or more of the great classes of foodstuffs—proteins, fats, carbohydrates, salts, vitamins and water, which together make up a complete diet.

In the case of proteins it is recognized that all the amino-acids are not of equal value in nutrition, for whereas certain acids, such as glycine, can be synthesized in the body, others, such as the aromatic amino-acids, cystine, and probably also the newly isolated sulphur-containing amino-acid, methioneine, must be given in the

diet, unless pathological changes are to follow. The absence of cystine in the food is associated, for instance, with loss of weight and gradual loss of hair. Gelatine, as is well known, represents a protein which is deficient in a number of amino-acids; but even when gelatine, supplemented by these amino-acids, is fed to rats as the sole source of protein, growth does not always occur, for many of the animals die with symptoms of an acute hæmorrhagic nephritis. (Jackson, Sommer and Rose, 1928.)

A deficiency disease which occurs in rats when fats are entirely excluded from the diet, has also recently been described by Burr and Burr (1929). The symptoms are necrosis of the tail and necrotic lesions of the skin. The disease can, however, be cured by the addition of 2% of fatty acids to the diet. An adequate supply of carbohydrate is also of importance as constituting the most economical method of insuring the necessary amount of energy-producing food in the diet.

A large number of mineral salts are also essential dietary constituents—calcium, sodium, potassium, phosphorus, iodine, iron, and probably, in very small quantities, copper and manganese—for in experiments on nutritional anæmias in rats it has been found that these two elements are of importance in the formation of hæmoglobin. Possibly a lack of copper and manganese plays a part in the causation of the obscure anæmias of the tropics, of which very little is yet known.

Finally, the ever-increasing number of vitamins requires consideration. Absence of vitamin A in the diet leads, as is well known, to keratomalacia and to changes in the epithelial cells of the respiratory and intestinal mucosa, as well as in the secreting glands associated with these structures. As a result of these changes bacterial infection is favoured, probably owing to the decreased content of the various glandular secretions in lysozyme.

A further vitamin factor, soluble in alcohol and ether, has recently been described by Coward, Key and Morgan (1929). It is present in "light white" casein and milk, and appears to be essential for growth, but little is yet known as to the pathological changes resulting from its absence.

Absence of vitamin C is associated with the development of scurvy in certain species of animals. Vitamin D, which is now known to be irradiated ergosterol, is responsible for the prevention of rickets. The ætiology of rickets is, however, more complicated than a simple deficiency of vitamin D, for it has been recently shown that it is possible to extract from certain cereal food-stuffs, such as oats, a substance which, when injected into animals, lowers the blood-calcium to such a degree that rickets results. Ovarian extract also has the power of lowering the calcium concentration of the blood. This explains why ovariotomy sometimes cures cases of osteomalacia. Certain foodstuffs may therefore contain anti-vitamins. A somewhat similar effect may occur with vitamin E, which controls fertility. Though fertilization and implantation of the ovum may occur in the absence of vitamin E, there comes a stage in development when the embryo collapses and disintegrates. According to Waddell, Steenbock and van Donk (1928) the incorporation of 1% of ferric chloride in an adequate natural diet leads to destruction of vitamin E. It is possible that anti-substances may be associated with the other vitamins.

There is finally the vitamin-B complex, which is of especial interest in connection with the diseases beri-beri and pellagra. First there is the thermolabile antineuritic factor vitamin B_1, absence of which from the diet of animals and birds, leads to symptoms of paralysis, associated with convulsions. There is also a second thermolabile factor according to Reader (1929), who claims that it is necessary for the growth of the rat. Williams and Waterman (1928) have, in addition, described a third thermolabile factor which is supposed to be necessary for the growth of pigeons, but not of rats.

In association with vitamin B_1, in many foodstuffs, such as yeast, there occurs a relatively thermostable factor, vitamin B_2, absence of which from the diet of rats

leads to dermatitis and to changes in the central nervous system. A condition resembling black tongue in dogs is also produced by a deficiency in this factor. Hunt (1928), on somewhat inadequate grounds, has described a second thermostable factor which he believes to be necessary for the growth of the rat.

In yeast there are also to be found two other substances which are of considerable interest from the point of view of nutrition. The first of these is bios, small quantities of which are apparently necessary for the growth of certain strains of yeasts in inorganic media. The second substance is one which prevents the onset of a curious disease in the rat, resembling pink disease in children. In 1927 Boas found that when young rats were fed on a diet in which the sole source of protein was dried egg-white, they developed a dermatitis and curious nervous symptoms. The pathology of this condition was investigated by Findlay and Stern (1929), who found that the pathological changes in the nervous system—round-celled infiltration into the cord and degeneration of the myelin sheaths of the peripheral nerves—were indistinguishable from those occurring in pink disease in children.

The similarities between pink disease in children and this syndrome in rats may be still further emphasized. Both diseases occur in young animals. Pink disease has never been recorded in children above the age of $3\frac{1}{2}$ years, while it is only after from three to five months on the diet of dried egg-white, that cutaneous lesions can be produced in the adult rat. Both syndromes may occur on a diet of mother's milk or on a ration containing all the known vitamins. The clinical symptoms of both diseases are nutritional, nervous and cutaneous. In rats there is a characteristic "kangaroo" position, in children a knee-elbow attitude. In both rats and children there is a curious mousy odour. Death is often due to an intercurrent broncho-pneumonia. The disease in the rat may be cured or prevented by the addition of dried yeast—but not marmite—to the diet. Fresh, but not dried, liver also has a definite curative action. Pink disease has now been recorded in children in Australia, America, most European countries and South Africa. It is probable that it will be found in the tropics also.

The pathology of vitamin B_1 deficiency in animals differs in certain respects from that of human beri-beri, which, as is well known, occurs in three forms, the wet, dry and cardiac types, which, however, may not be sharply differentiated. In birds fed on a diet lacking in vitamin B_1 there occur paralysis of the legs, wing-drop, and finally, convulsive movements of the head, associated with opisthotonos. In rats there is also motor paralysis and in some cases convulsive seizures. Pathologically, there is found a myelin degeneration of the nerve-sheaths in birds, but not in rats. This myelin degeneration in birds appears to be associated with the general starvation rather than the lack of vitamin B_1, for it is found in animals fed solely on marmite, which contains B_1.

Generalized œdema and hydropericardium are not commonly met with in animals subjected to a deficiency of vitamin B_1, but McCarrison (1928) has found that œdema together with hypertrophied right heart may occur in pigeons fed on a diet containing small quantities of vitamin B_1. In America it has recently been found that rats fed on a similar diet have an increased water content of the tissues. The chief symptoms of human beri-beri can thus be reproduced in animals. The curious convulsive movements of birds on a diet lacking vitamin B_1, however, are not seen in man. These convulsive movements are possibly a sign of anoxæmia, for they can be reproduced by the injection of sodium nitrite, or potassium cyanide, or by inhaling carbon monoxide.

It seems probable that in certain instances true beri-beri in man has been confused with two other conditions associated with œdema—nutritional œdema and epidemic dropsy. The former condition is probably due to some form of protein deficiency, but it has never been reproduced in animals, although it occurs regularly in man, in association with famine conditions, as in Russia in 1921. Epidemic dropsy is

probably quite distinct from beri-beri, for it appears to be largely restricted to India, whereas beri-beri has been recorded from this country and is not uncommon among peoples who do not live upon rice at all. Epidemic dropsy does not occur in breast-fed infants, whereas the wet form of beri-beri does. Some years ago in the Philippines it was shown to be possible to produce the wet form of beri-beri in puppies by feeding them on the breast-milk of women whose children had developed beri-beri, although the women themselves had no signs of active beri-beri. It is difficult to imagine a toxin which could be excreted in the milk in such large amounts as to cause beri-beri in the children while leaving the mothers unaffected. It is simpler to suggest that there is in the mother's tissues a deficiency of some factor, the same deficiency being intensified in the milk.

In epidemic dropsy there is often an acute erythematous rash on the skin, while glaucoma has not infrequently been described. Very frequently also, epidemic dropsy has an explosive onset. But if, as is suggested, this condition is due to a toxin formed from the rice, akin perhaps to that in ergot poisoning, it should not be difficult to obtain this so-called bad rice and to feed animals on it, thereby causing the typical symptoms even in the presence of vitamin B_1.

When rats are fed on a diet deficient in vitamin B_2 nervous symptoms do not occur, but there is a characteristic dermatitis, with a hæmorrhagic discharge from the nose, and frequently the passage of blood in the urine. Pathologically, the changes in the skin and tongue of these rats are closely akin to those of human pellagrins. Changes are also found in the central nervous system of the rats, vacuolation and shrinking of the cells of the anterior horn, and later, the collection of lipochrome pigment (Stern and Findlay, 1929). Degenerative changes in the cord are not found, but neither do they occur in human pellagra until the case has become chronic.

Experimentally, therefore, a disease can be produced in the rat, unassociated with the eating of maize, which is not dissimilar to human pellagra.

BIBLIOGRAPHY.

Boas, M. A., *Biochem. Journ.*, 1927, xxi, 712. Burr, G. O., and Burr, M. M., *Journ. Biol. Chem.*, 1929, lxxxii, 345. Coward, K. H., Key, K. M., and Morgan, B. G. E., 1929, *Biochem. Journ.*, xxiii, 695. Findlay, G. M., and Stern, R. O., *Arch. Diseases in Childhood*, 1929, iv, 1. Hunt, C. H., *Journ. Biol. Chem.*, 1928, lxviii, 83. Jackson, R. W., Sommer, B. E., and Rose, W. C., *Journ. Biol. Chem.*, 1928, lxxx, 167. McCarrison, R., *Ind. Journ. Med. Res.*, 1928 (Memoir No. 10), p. 1. Reader, V., *Biochem. Journ.*, 1929, xxiii, 689. Stern, R. O., and Findlay, G. M., *Journ. Path. and Bact.*, 1929, xxxii, 63. Waddell, J., Steenbock, H., and Van Donk, E., *Journ. Biol. Chem.*, 1928, lxxx, 431. Williams, R. R., and Waterman, R. E., *Journ. Biol. Chem.*, 1928, lxxviii, 311.

Dr. H. B. Day said that pellagra and beri-beri were not associated. Symptoms of pellagra did not occur in a case of beri-beri or vice versa, so far as he knew. Pellagra bore the same relation to the consumption of maize as did beri-beri to the consumption of rice. Much depended, apparently, on the vitamin deficiency.

He did not know how long pellagra had existed in Egypt; Sandwith had described its occurrence there in 1893, and found evidence that it had existed a considerable number of years. He (the speaker) placed it high in the list of the modern plagues of Egypt. All, or almost all, the theories in this discussion concerning beri-beri had been advanced in the case of pellagra. Opinion veered for a time between that of maize being a deficient diet for man, and the view that in damaged maize, owing to the growth of a fungus, toxins were produced which were responsible for the appearance of pellagra.

Shortly before the European War the infection theory of pellagra gained a number of adherents. This theory was suggested by the almost epidemic outbreak of pellagra which occurred in some of the Southern United States. Sambon sought for an insect transmitter, but no one had succeeded in transmitting the disease. Goldberger tried the experiment on prison volunteers, but did not succeed. The modern study of pellagra dated from the experimental school with food experiments on animals, from the opportunity that the spread of pellagra in America gave to the

investigators there, and lastly, in Egypt from the circumstances of the European War, when pellagra occurred in conditions which could be controlled. During the war, a number of Turkish prisoners were assembled in camps near Cairo, and in those camps pellagra made its appearance. These men were kept on a known diet; the history of the patients could be taken, the progress of the disease observed, and measures of prevention or cure carried out. A special Commission was appointed in relation to it, and made a report. The clinical features of pellagra were well seen in this epidemic. The first symptom favoured the idea of an infectious origin, namely, diarrhœa. This had nothing very characteristic about it, as Dr. Manson-Bahr found, unless the disease was complicated by *Entamæba histolytica* or other condition such as bilharzia. In some cases the stools resembled those in sprue; they were acid and highly fermentative. The general symptoms included weakness, mental depression, tenderness, etc., and then followed the rash, two to four months later, usually in the spring. He did not know whether that was because the actinic rays of the sun had then more influence. It could be regarded as an aggravated form of sunburn, and it corresponded to the experimental condition seen in rats.

At first the nutrition did not suffer, but the blood-pressure was distinctly lowered, being generally under 100 mm. The central nervous system was involved; the deep reflexes were increased at first, later they might be lost. A slow degeneration of the cerebral centres was noted, and often progressed to dementia. Parotitis also might appear, with great chronic enlargement of the parotid glands, but he had no proof that this was solely due to the pellagra.

The cause of pellagra was connected with nutrition, chiefly of the ectodermal structures—skin, mucous membrane of the intestinal canal, and the central nervous system. The skin atrophy was chiefly seen in the parts which had been invaded by the rash. A case could be recognized as one of pellagra after the rash had gone. The tongue showed a glazed condition, much like the very clean tongues seen after scarlet fever. Deprivation of vitamin B led to atrophy of the intestinal mucosa and dilatation of the stomach, and it was probable that this mal-digestion and mal-assimilation of food completed the vicious circle initiated by the defective food. Pellagra was not so much an acute disease as a chronic condition.

The Pellagra Commission in Egypt devoted a good deal of attention to the biological value of proteins in the diet, calculated according to the amino-acid content. It was known that maize was deficient in tryptophane, that 102 grm. of maize contained the equivalent of 30 grm. of meat, and so one had to give far more vegetable protein. After the Report was published some doubt was cast on it, because the Commissioners had relied on a comparison of the respective diets of Turkish and German prisoners of war. Turkish prisoners developed pellagra, but German prisoners did not. After the Report was issued, however, pellagra broke out among German prisoners, though on a much smaller scale. In both cases an increased dietary stopped the outbreak and restored the patients.

Further work had been done on pellagra, especially by Goldberger in America, who found in asylums and other institutions in Carolina and Tennessee, where pellagra was endemic, that it might be prevented by a more liberal and varied diet, i.e., with the addition of meat or buttermilk. Butter and casein, however, had little effect upon it. Therefore it was suspected to be due not to a mere protein deficiency, but to the lack of a special constituent. By finding the preventive action of yeast, and its curative action in polyneuritis of birds, Goldberger was led on to the separation of the vitamin complex into B_1 and B_2; because an 85% alcoholic extract of yeast would cure polyneuritis or prevent it, and animals, such as rats, which remained free from polyneuritis developed a condition of dermatitis resembling that in pellagra. The same worker studied the "black tongue" found in dogs fed on similar experimental diets.

On studying the subject it became clear that the problem in man was not the same as in animals; that each animal had a different liability to food deficiency. Pigeons could do without B_2, but rats could not; and probably man had a different susceptibility from that of any of the animals used in experimentation.

Work had been done on the question of relation of the vitamins to the total protein consumption, and it had been suggested that a larger protein consumption needed more vitamin B than when the protein was cut down to a minimum. That might explain why there were vagaries in this condition. Vitamin B seemed to act in the body like insulin; it was required for the due assimilation of foodstuffs.

Dr. G. W. Bray spoke of the occurrence of infantile beri-beri in the Mandated Territory of Nauru, in the Polynesian group of islands off New Guinea, under the control of the Commonwealth of Australia. In earlier years 50% of the infants died under the age of one year; in one year of his inquiry thirty out of sixty infants died in the first few months of life. The natives did not eat rice; they ate coconut products, fish, and native fruits. They were prohibited by the Government from consuming fermented liquors. For variety they ate tinned meats, oatmeal, and cornflour, substances which contained no "B" factor.

The diagnoses formerly made ranged from "stomach trouble" to marasmus and broncho-pneumonia. Usually the deaths occurred from the ninth to the eleventh week. They were fewest at times of greatest rainfall, so that there seemed to be a close relation to the food supply. The infants were brought with a history of vomiting and screaming, and then death would occur in about five minutes. In most of the cases the actual illness did not last longer than twenty-four hours. The first symptom was abdominal distension and vomiting, then the child passed into rigidity, convulsions and death. A chronic type was that associated with constipation. In the acute case there was a progressive gain in weight to a point, then the onset of the symptoms and death.

The substance found to be most beneficial in these cases was the yeast grown in the sap of the coconut palm. The use of this for babies had resulted, in three years, in wiping out the great death-rate.

With regard to the appearances, there was a huge liver, the stomach was markedly distended, and the heart greatly dilated, especially on the right side.

The blood-picture was that of a leucopenia. The small lymphocytes disappeared from the blood. The mother's milk was found to be deficient in fat. The curative sap, or "toddy," fermented, and a layer of yeast formed in the bottom of the vessel. It was emulsified with cod-liver oil and was administered to the children daily. Since this treatment was inaugurated there had been only one death from the disease, and the average weight was now 19 lb. at the age of 6 months, whereas previously it was 19 lb. at the age of a year, on the average. Moreover, the condition was formerly responsible for from thirty to forty admissions to hospital per month, whereas there were now no admissions due to this cause.

Dr. Tertius Clarke said that in his opinion there were two diseases. The disease encountered in Malaya was true beri-beri; the disease seen in India was not. Dr. Findlay had said this evening that dry beri-beri was rare, but in his (the speaker's) experience, in Malaya it was common. An appropriate diet completely checked it. It had been rife in the jails, but when parboiled rice was given in place of the polished rice, it ceased. Unless the patients in hospital were practically moribund, their recovery on the appropriate diet was very rapid, though it had no effect on the residual paralysis. He did not think that for bringing about a cure it was essential to have actual parboiled rice; any rice which was not polished would prevent the disease. Kedah was a rice-producing country, without any importation of it, and there was no beri-beri. The rice was not polished or parboiled. The

nationalities in Kedah were the same as in other parts of Malaya, namely, Malay, Chinese and Tamil.

The Norwegian worker, Holst, said—and it was true—that in every acute case of beri-beri examined after death, a duodeno-enteritis was found, and sometimes there was inflammation of the stomach as well. Possibly the intestinal lesion was secondary to the nerve lesion, and any further lesion entirely secondary.

With regard to the theory of endocrine irregularity, there was the significant point that if one took a group of forty or fifty cases and changed their diet, the disease disappeared.

Dr. W. R. Aykroyd said he had recently observed cases of beri-beri in people who were on a staple white-flour bread; that was, beri-beri as it occurred in Newfoundland and Labrador. In those countries the disease was never regarded as different from the tropical rice-eaters' variety. For practical purposes the two diseases seemed to be identical. As seen in the countries he named, beri-beri might be defined as a polyneuritis associated with myocarditis, and occasionally with œdema, which occurred in people suffering from malnutrition, and responded to dietetic treatment. For three or four months each year the diet of sufferers was almost restricted to refined white-flour bread, with the very small addition of such foods as salt meat (beef and pork), molasses, and one or two other minor articles of food. In Newfoundland and Labrador one found beri-beri in the poorest families; it was a poverty disease. In the more northerly parts of the country the people had to buy enough food in December to last about six months, for during that time they were practically marooned. Those who were reasonably well-off bought, in addition to flour, other foods to give variety, such as turnips, onions, potatoes, etc. The seasonal incidence of the disease was very clear-cut, most of the cases occurring in April, May and June, the worst dietetic period of the year; few cases occurred in late summer and autumn, when fresh fish and meat were available. The question of bad flour as a possible factor in beri-beri did not arise in those parts, because wheat flour did not readily deteriorate, and the whole population was supplied with much the same kind. The fact that obvious beri-beri occurred on a white-flour staple was strong evidence of the truth of the deficiency theory.

With regard to the exact relation of beri-beri to deficiency of vitamin B_1 the disease as he saw it in North America, confirmed such a relationship. In 1912 Little, who worked there, observed that at one part of the coast a cargo of wholemeal flour was wrecked, and the people obtained possession of this flour and used it. In that season beri-beri had shown a tendency to disappear in that region. People who had a good supply of potatoes seldom had beri-beri, and potatoes contained a fair amount of vitamin B_1. In Labrador, where the people were poorer, beri-beri had always been comparatively rare, because a supply of fresh meat was usually available; fresh meat, a source of the vitamin, seemed to check the onset of beri-beri. Treated on a proper diet containing excess of vitamin B_1 a sufferer from beri-beri would usually be fit for work in four months. In his experience, wheat-germ and yeast could be given to patients without producing much effect, unless an all-round improvement was made in the diet. When a patient had been on a diet generally deficient, as were most beri-beri producing diets, he would be more likely to respond to a good all-round diet than to a vitamin concentrate.

Most of the cases of beri-beri in the countries he had mentioned were of the dry form. Possibly the wet form was beri-beri *plus* hunger œdema, a condition perhaps due to protein deficiency.

There were a few points which could not be explained on the deficiency theory. One was the immunity of children between the ages of 2 and 15 years to beri-beri. Another was the occasional occurrence of cases of what seemed to be beri-beri under

conditions of a fair diet. These cases were very rare. In the majority of cases the relationship to faulty diet was very clear-cut.

Dr. H. S. Stannus asked if Dr. Findlay would give some idea of the way in which food deficiency produced the symptoms. Was it not possible that the deficiency of an accessory food factor might unmask some definite physico-chemical action, i.e., in the absence of some vitamin, some substance from within or without the body might act as a toxin? The onset of rickets was facilitated by giving oatmeal in large quantities. He would also like to hear the explanation, in the acute, beri-beri in children, of what happened at the moment on onset of acute symptoms, the child "screamed, vomited, and died." He did not understand how the *absence* of anything could produce such symptoms, which resembled rather those of an acute toxæmia.

He was familiar with pellagra, and the changes in the nervous system in that disease were comparable with those seen in toxic conditions, as shown by Kinnier Wilson in material he had sent him from Central Africa. It was suggested that the toxin entered the nervous system along the posterior root-sheath lymph channels.

He wondered whether different species of animals made use of different amino-acids. Was it reasonable to suppose that individuals of a particular tribe or race who had subsisted on a particular diet since childhood, made use of only certain amino-acids, and that if the diet were changed disease might result? Some natives went sick when their diet was changed, apart from the question of vitamins.

Dr. J. Kingston Barton said that it was the custom in many tropical countries to keep children to the breast until they were one or even two years old. Could Dr. Bray suggest why the breast-fed children in Polynesia should have failed so soon? He (the speaker) supposed that the breast-feeding in those cases, owing to the poor condition of the mother, was practically continuous starvation.

Dr. Bray, in reply to Dr. Kingston Barton, said that the children had not shown any rise of temperature, and their motions had been normal. There was diarrhœa, but the blood-picture did not fit in with that of a toxæmia, as there was leucopenia affecting only the small lymphocytes. In most of the cases investigated, the diet of the mother had been mere sugar-water; she would drink 1½ pounds of sugar in water per day without eating native food. The consumption of huge quantities of this sugar-water caused a polyneuritis. After the use of the "toddy" which he had mentioned the symptoms would sometimes clear up within an hour, and the child begin to thrive. Toddy had been disallowed by the Government, but it was reintroduced, though with the proviso that it must not ferment for long. No infantile beri-beri had been reported as occurring in the island for the last three years, and the infant mortality had been reduced from over 400 per 1,000 births to about 70, which was not much worse than the figure for England. Steps had now been taken to restrict the use of so much sugar.

White flour was not sold in any native stores, and polished rice was not allowed to be sold, but the stores were required to keep brown rice with a phosphorus content, and wholemeal flour and bread were used on the island.

Dr. J. B. Christopherson (Chairman) remarked that Dr. Stannus's work had been done in Nyasaland, where he (the Chairman) thought there was a good deal of pellagra. His own experience of tropical diseases had been in the Sudan, where pellagra was seldom met with, though in the neighbouring country of Egypt pellagra was one of the national diseases, and one of the most serious. In the Sudan, millet was the staple food, and in Egypt, maize. He would like to know how Dr. Stannus accounted for the amount of pellagra in Nyasaland.

Dr. Stannus (in reply to the Chairman) said that the outbreak of pellagra in Central Africa which he had investigated was in a prison, in which the ration consisted of rice and salt. There was an arrangement in regard to the prisoners whereby some of them were allowed visits from their wives. Among the prisoners who had their wives in attendance the sick-rate was much less than among the other prisoners, and the only explanation which seemed to account for it was that the wives were allowed to take the rice and salt ration away to barter for other varied articles of diet, which were then supplied to their prisoner husbands. Pellagra occurred among those who ate little but rice. The prisoners' ration was a poor one in every respect.

Reverting to Dr. Bray's remarks, he suggested that the milk of mothers on a diet of sugar and water might have been toxic, and so produced the acute condition in the infants in the absence of the vitamin.

Dr. G. W. Theobald said that, with regard to Professor Megaw's naive statement that whatever the cause of beri-beri might be, the treatment was simple, and merely consisted in prohibiting rice and giving a varied diet, he (the speaker) had found that "simple treatment" impossible in practice. He had seen a considerable number of cases of beri-beri, all associated with pregnancy. They were of the dry type, with one exception, and all improved on the ordinary diet and vitamin B. The patients did not suffer from any dilatation of the heart, or cardiac symptoms. He did not see any fundamental difference between that form of beri-beri and the kind produced in pigeons by McCarrison and other workers. What impressed him most was that Siam, the third greatest rice exporting country in the world, and one which existed on the revenue from its rice, should have to polish it for the London market. The prodigal son "would fain have filled his belly with the husks that the swine did eat." In modern Siam, the Government would fain fill the bellies of their people with an expensive extract from the husks which were, indeed, given to the swine to eat. It was true to say that the London market was the cause of beri-beri in Siam. He earnestly hoped that some authority—perhaps the League of Nations—would tackle this and similar urgent problems in the near future.

Major-General Megaw (in reply) said that Dr. Aykroyd had told him privately that he had seen a condition resembling epidemic dropsy among people who did not eat rice.

Dr. Findlay said that infantile beri-beri could be explained more readily as a deficiency in the mother's milk than as due to the excretion of a toxin in the milk, but he saw no reason why a toxin should not be excreted in the milk of the mother. In epidemic dropsy he had not seen anything which could be called a true rash; there was sometimes a vascular mottling on the surface of the skin. He had seen this condition described by Japanese writers as being common in beri-beri. Glaucoma did not occur in beri-beri, though French writers described a scintillation of the eyes and dimness of vision. It was true that epidemic dropsy usually occurred as an explosive outbreak, but it was not always so, and, not infrequently, beri-beri also appeared as a definite outbreak.

Dr. Findlay had placed his finger on the weak spot in the argument in favour of epidemic dropsy being an intoxication when he asked why we had not found the toxins. He (Major-General Megaw) suggested that these toxins were very elusive, not only in this but in many other diseases. In epidemic dropsy the manifestation was not seen until several days after the food had been taken; often the patient had been taking small quantities of the poison over a long period. It was difficult to get samples of the rice which was the cause of the illness as the rice had often been consumed before the disease was recognized. The cause could not be said to be vitamin deficiency, because the patients had been eating a diet which was satisfactory in all respects.

With regard to the analogy between beri-beri and pellagra, here were two deficiency diseases, each closely associated with the eating of a certain article of food. He had been surprised to hear Dr. Stannus say he had come across an outbreak of pellagra among people who were eating rice, as something like 95% of the cases of pellagra occurred in eaters of maize, while at least 95% of the cases of beri-beri were in rice-eaters.

He did not know how to account for the infantile beri-beri in Polynesia, but the description given by Dr. Bray showed that it had been carefully studied, and if such studies were carried out oftener, an accurate knowledge of disease processes would be more quickly obtained. Probably the gastro-intestinal irritation referred to by one speaker was an early manifestation of beri-beri; its occurrence suggested that an irritant toxin entered the body through the gastro-intestinal mucous membrane.

Dr. Findlay (in reply) said that those who still believed that beri-beri and pellagra were due to toxins produced from bad rice and maize were faced with the difficulty that these diseases sometimes occurred in people who did not eat rice or maize. It would be necessary, therefore, to imagine the characteristic toxin from rice or maize formed in association with entirely different foods.

With regard to the question of a toxin in the milk in infantile beri-beri, there was no evidence that in a disease such as ergotism any toxins were excreted in the milk by which the suckling child could be affected. In scurvy, on the other hand, it was well known that the young could be affected by a deficiency of vitamin C in the mother's diet, and the same was almost certainly true of beri-beri. Dimness of vision which sometimes occurred in association with beri-beri, was probably due to lack of vitamin A, in which rice was also deficient.

In reply to Dr. Stannus, it was not known how vitamin B_1 acted. There was evidence to show that metabolism was interfered with by its absence in a number of ways. The metabolism both of proteins and fats appeared to be affected, possibly there was anoxæmia or a change in the oxidation reduction potential of the tissues. There were, at any rate, many ways in which a toxin might be formed in the body as the result of faulty metabolism.

With regard to the production of definite skin changes by vitamin B_2 deficiency, it had been known for many years that pellagrins were more sensitive to sunlight than ordinary people. It was not sensitization to ultra-violet light in the way that hæmatoporphyrin caused sensitization, because any stimulus would cause the onset of dermatitis. In the United States there had been cases in which exposure to X-rays had precipitated a pellagrous dermatitis. Pressure would give the same effect; a person wearing a tight belt showed dermatitis on the pressure area. Thus there was an increased sensitivity to stimuli and liberation of some s ubstance resembling histamine, which set up the vascular reaction and the subsequent desquamation.

Dr. J. B. Christopherson (Chairman) said that the problem of these diet-deficiency diseases, beri-beri and pellagra, was most important to countries like India and Egypt. It was to be hoped that when India and Egypt gained that measure of political independence which they sought, they would not lose sight of these great medical questions, but would carry on and extend the investigations into those problems which had been pursued, with native help, with such success in the past.